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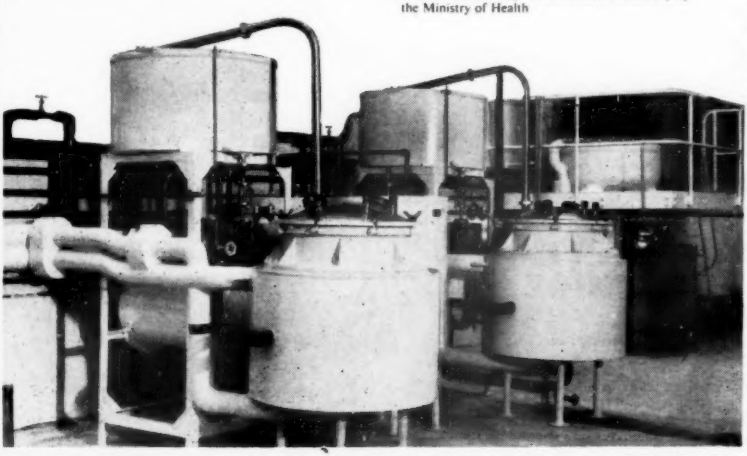

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PROCEEDINGS
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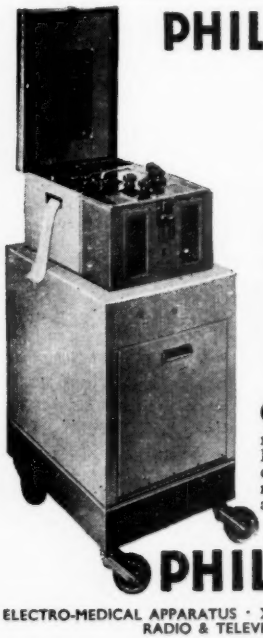

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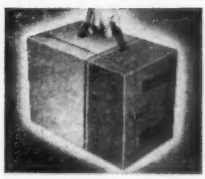

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*Proceedings of the Royal Society of Medicine* Vol. 47 75

# Section of Proctology

President—T. McW. Millar, F.R.C.S.Ed.

[*November* 11, 1953]

## John of Arderne, The Father of British Proctology

PRESIDENT'S ADDRESS

By T. McW. Millar, F.R.C.S.Ed.

*Surgeon, The Royal Infirmary, Edinburgh*

John of Arderne was born in 1307 and died in 1390. He lived for 83 years—an unusually long span for those days—and his 83 years covered a large part of the fourteenth century—the Middle Ages, 200 years before the Renaissance, more than 100 years before Columbus discovered America.

England was then a country of strange contrasts, a country which had already seen the building of some of the great cathedrals, such as Salisbury, still fortunately preserved for us, but a country of little domestic architecture, except for the fortified castles of the great lords; a country with bad highways beset by robbers, with deep fords and ill-mended bridges. Socially and intellectually the period was an age of unrest, when the manorial system was beginning to break up with the freeing of the serfs and villeins, and new classes of farmers and merchants and labourers were beginning to make their appearance. It was, we learn, an age of strikes and uprisings. It was the century in the middle of which (1349) occurred the scourge of the Black Death, which is believed to have killed in the course of two years at least one-third and possibly one-half of the population.

It was moreover the age of chivalry, of knights in armour and fair ladies. The century covered the greater and, from the English point of view, the more successful part of the Hundred Years War, "which enriched individuals with plunder and ransoms from France, and swelled the luxury of Court and Castle, but was a curse to the Country as a whole" (Trevelyan). It embraced the reigns of Edward I, the Hammer of the Scots, of Edward II on whose forces suitable punishment for his father's misdeeds was inflicted at the Battle of Bannockburn, of Edward III and of Richard II the son of the Black Prince, "the strong and warlike lord" as John of Arderne himself describes him.

Chaucer was born some twenty years after John of Arderne and lived to the end of the century. For the first time the modern was mingling with the mediæval in literature and Chaucer's writings were registering the greatest development of all, "the birth and general acceptance of our language, the Saxon and French words happily blended at last into the 'English Tongue' which all could understand". The more learned of the clergy, and some others including our hero, had Latin, and Arderne's works are written in that language. One hundred years had still to pass from the time Arderne wrote his treatises till William Caxton set up his printing press at Westminster, under the shadow of the Abbey.

Finally, to complete the background picture it may be appropriate to try to sketch the state of medicine, and particularly of surgery, in those mediæval times. The Arabian School of Medicine had held sway from the fifth to the eleventh century; it was succeeded by the School of Salerno which probably came into existence in the ninth century. By the twelfth century men trained at Salerno had begun to found schools elsewhere, in France, Spain, Portugal and England, and the

period from the early twelfth century to the middle or latter half of the fourteenth century saw a great efflorescence of learning, marked by the establishment of no fewer than some 30 universities throughout Europe. It is probable that this pre-Renaissance was brought to an end by the paralysis which followed the Black Death. Then ensued a period of retrogression until in the fifteenth century the Renaissance itself blossomed in the great Italian schools of Padua, Bologna, Ferrara and Pisa.

John of Arderne was born therefore towards the end of the brilliant period of the pre-Renaissance. It is believed that he was educated at Montpellier in France, near the Spanish border, a university which, when he attended it, would have been in existence for some 200 years. There he would probably come under the influence of two outstanding surgeons, Henri de Mondeville (1260–1320) and Guy de Chauliac (1300–1368).

Henri de Mondeville is a notable figure in the history of surgery. He had inherited from Theodoric (1205–1296), one of the most original surgeons of all time, the principle originally taught by Hippocrates of avoiding suppuration in wounds by simple cleanliness. According to Allbutt, after Theodoric only de Mondeville and Paracelsus (1493–1541) upheld this principle till, 600 years later, it was finally triumphantly vindicated by Lister. In this long interregnum the advocates of suppuration won all along the line.

De Mondeville is described as a hardy and original thinker. He left for posterity a surgical treatise which abounds in directions of the rarest common sense for the aseptic treatment of wounds, and in shrewd practical advice as to the conduct of a surgeon's professional life. Although we are told that his writings contain many verbose maunderings, they also include such biting utterances as "God did not exhaust all his creative powers in making Galen", and "Keep up your patient's spirits by music of viols and ten-stringed psaltery, or by forged letters describing the death of his enemies".

Guy de Chauliac (1300–1368), a contemporary of Arderne, is described as the most erudite surgeon of his time and the most eminent authority on surgery in the fourteenth and fifteenth centuries. His ethical standards were much higher than those of de Mondeville. His operations were based on a study of human anatomy and many of his methods of treatment were surprisingly modern, such as the excision of cancer at an early stage by the knife, the suspension of fractures and even the treatment of thigh fractures by means of weights and pulleys. Unfortunately in the important matter of the treatment of wounds he was a reactionary, supporting as he did the doctrine that the healing of a wound must be accomplished by the surgeon's interference rather than by the healing power of nature. As an abridged version of his most important work, published in many editions and translations, became the vade-mecum of surgical practice and remained so even after the sixteenth century, for hundreds of years his reactionary teaching on wound treatment exercised a baleful influence on surgical practice.

Such then were the men from whose writings, and possibly even from whom in person, our John of Arderne learnt his surgery. Of Saxon descent himself, he must have come fully under Norman and French influence. He served in France in the earlier part of the Hundred Years War, very probably attached as a surgeon to the Duke of Lancaster. He is believed to have been present at the Battle of Crecy (1346) and to have returned to England soon thereafter—a well-trained, experienced and successful surgeon with, what was probably of great importance, many influential friends in high quarters. He married, for it is on record that in 1348, jointly with his wife, Ellen, he bought 18 acres of land in Mitcham in Surrey for the sum of six shillings and eightpence. There is a further record that he sold this land in 1351. In this record there is no mention of his wife, and nothing more is heard of her. D'Arcy Power suggests that she may have died in childbirth or more probably of the Black Death. Thereafter he went to Newark in Nottinghamshire, then an important centre and a meeting place of Parliament. He himself records, "I dwelled in Newark in Notts from the first pestilence that was in the year of our Lord 1349 unto the year of our Lord 1370". During these twenty-one years he would appear to have conducted a large and successful surgical practice, probably living under the patronage and protection of the Duke of Lancaster and later of John of Gaunt. In 1370 he moved to London, being then 63 years of age, and there he lived till he died twenty years later. It was after his return to London, when he had already acquired his extensive experience, his surgical skill and his knowledge of men and affairs, that he began to write his treatises.

We know little of Arderne except what we learn from his own writings. There appear to be only a few references to him in other works, and these relate to his fame as a pharmacist rather than to his reputation as a surgeon. But the man is revealed to us in his own writings, and the picture emerges of a well-educated gentleman of high ethical principles, of a doctor of wide understanding who cared well for his patients, of a surgeon with an original mind who was a highly competent operator and of a writer who had the power of graphic and accurate description.

His writings consist of a number of treatises each dealing with a different branch of medicine or surgery. Each treatise was written as a separate work or monograph and could be acquired separately, but taken together they form a fairly complete system of surgery as it was known and understood in these days, when surgery had not yet been divorced or separated from medicine and when neither had freed itself from the herb-lore of Saxon times. Each treatise was written in Latin "in his own

hand and copied or translated into English by scribes from both the north and the south; and judging from the number of manuscripts still preserved in libraries—over 60 in all—it would appear they were widely read for perhaps some 150–200 years. His whole works were later collected into a portly volume, of which two copies still exist, the "Practica Magistri Johannes de Arderne" (Figs. 1 and 2).

The subjects covered in the various monographs are: Hæmorrhage, Diseases of the Eye, Diseases of the Male Generative Organs, Diseases of Women, Diseases of the Kidneys, Intestinal Obstruction, Gout, and one of interest to proctologists, "A tretis extracte of Maistre John Ardern of Fistula in Ano and of Fistula in other places of the body and of apostemes making fistules and of emoraides and tenasmon and of clisteres: of certayn oyntementes, poudres and oyles". Finally there is a

FIG. 1.—From an early fifteenth century manuscript of the Practica Magistri Johannes de Arderne. (Reproduced by kind permission of the British Museum and the *British Journal of Surgery*.)

supplement—a kind of case-book in which are described a series of interesting cases. The great merit of the system, as Sir D'Arcy Power points out, is that the author writes from a clinical standpoint, the general scheme of each section being to illustrate the diseases described and the management of these from personal experience and to give details of the patients—often mentioned by name—whom the author has treated.

The status of John Arderne as a surgeon is clearly described by Sir D'Arcy Power in his foreword to the Treatise on Fistula in Ano, published in 1910: "The position which Arderne occupied was perfectly well recognized both in England and France, and was identical with that which we occupy at the present time as consulting and operating surgeons. In France such surgeons were known in Arderne's time as surgeons of the long robe, to distinguish them from the barbers practising surgery, who were surgeons of the short robe. In England the prefix Master indicated the difference, and John Arderne is careful therefore always to style himself Magister Johannes de Arderne, Magister being his title as Master of Surgery, which distinguished him, on the one hand, from the Doctor of Physic who was his superior, and, on the other, from the Barber and the Apothecary who ranked below him" (Fig. 3).

In a section of the monograph on ano-rectal conditions, Arderne writes delightfully on the qualities required in a good and successful surgeon, and gives his advice on the behaviour of a surgeon towards his patients. This is a human and enlightening document. It shows that Arderne himself conducted his practice on high ethical principles, but it also shows that he had a great deal of worldly wisdom. Some detailed consideration of this section on "The Manere of the Leech" may prove of interest. Among the qualities he regards as necessary in a good surgeon are piety—"that he set God afore evermore in all his works, and evermore call meekly with heart and mouth his help",—charity—"and some time visit of his winnings poor men",—and modesty—"that he be not founden temeraries or boastful in his sayings or in his deeds". Next he enjoins the surgeon to be grave, studious and

sober. He should not be cynical—"Scorn he no man, for of that it is said 'he that scorneth other men shall not go away unscorned' ", and in his dealings with his colleagues he is advised to be courteous and not jealous. "If there be made speech to him of any leech, neither set he him at nought nor praise him too much or commend him, but thus may he courteously answer: 'I have not much knowledge of him, but I learned not nor have I heard of him but good and honeste'." He is warned to be continent and chaste, friendly to servants and easy of address, neither too rough nor too familiar.

He gives wise advice on the selection of patients. Never should the leech undertake the care or cure of a patient "but he see first the sickness and the manner of it; and when he has seen and assayed it, and it seem to him that the sick may be healed, nevertheless he shall make prognostication to the patient of the perils to come if the cure be deferred". Time and again he advises his surgical readers not to undertake the cure of a patient suffering from what was regarded as an incurable condition, and in this category he places certain cases of fistula-in-ano as we might do to-day, and cases of

FIG. 2.—From "De Arte Phisicali et de Cirurgia" of Master John Arderne. In the centre column the upper illustration shows one of Arderne's instruments for the operation of fistula-in-ano; the lower represents the contemporary idea of the skeleton. In the right-hand column the two lower figures represent patients suffering from prolapse of the rectum and pruritus ani. (Reproduced by kind permission of Staples Press Limited.

cancer of the rectum. He is wise and cautious about giving a prognosis and advises that, when asked by the patient or his friends how long the cure will take, the surgeon should state about double the time he expects, "for it is better that the term be lengthened than the cure, for prolongation of the cure giveth the cause of despairing to the patients"; and if the cure be speedy or of normal length the credit is to be given to the patient "for that he was strong-hearted and suffered well sharp things, and that he was of good complexion and had able flesh to heal".

Arderne appreciated the effect of the mind on the body and recommends surgeons to have a store of comfortable sayings and a stock of good stories, wherewith to cheer and encourage their patients, but on the other hand he warns against saying too much for, as he quotes, "It is more seemly to use the ears than the tongue", and again, "If thou had been silent thou had been holden a philosopher". All this advice on the duties and proper behaviour of a surgeon cannot be looked on as an original contribution from Arderne, for it was apparently the custom of mediæval surgeons to deal in their writings with this aspect of a surgeon's life. Thus William of Salicet and Lanfranc, the founder of

FIG. 3.—A fourteenth century surgeon (possibly John of Arderne) operating for fistula-in-ano. (Reproduced by kind permission of *St. Bartholomew's Hospital Journal*.)

French surgery, and above all de Mondeville wrote at considerable length on these subjects and it would appear that Arderne was familiar with their writings and followed their example, and probably borrowed their precepts in composing his rules for a surgeon. He also followed them in giving advice on the matter of fees, although, compared with others, he was very brief on this point, and very reasonable. Thus, when the surgeon sees his patient, "Pursue busily the cure (making good progress) as he boldly more or less, but ever should he beware of scarce asking, for over-scarce asking setteth at naught both the market and the thing. Therefore" (he continues) "for the cure of a fistula in ano, when it is curable, ask he competently, of a worthy man and a great, 100 marks or 40 pounds, with robes and fees of 100 shillings yearly for life". For a lesser man he advises a lower fee, but never should he take less than 100 shillings, "for never in all my life took I less than 100 shillings for cure of that sickness". Then follows a remark that seems to be typical of Arderne for it occurs more than once in his writings and marks him out as an honest man with an open mind, "Nevertheless do another

man as him think better and more speedful". As D'Arcy Power points out, "Arderne's teaching on the duties of a surgeon compares very favourably with that of Wm. Salicet and de Mondeville. He had a high moral tone, or at any rate, based his warnings on morality rather than upon self-interest". Arderne, for example, did not find it necessary to advise, as Salicet did, that a wise surgeon will do well to refrain from stealing anything while he is in attendance on a patient; or as de Mondeville did, that the surgeon should haggle with his patient over the size of his fee; or to make the statement, attributed to de Mondeville, that from time immemorial it has been an article of faith with the common people that every surgeon is a thief, a murderer or a swindler!

There are three aspects of his surgical technique that mark Arderne as a surgeon in advance of his time and as one of the important figures in the development of surgery in this country. I refer to his surgical cleanliness, his principles of wound treatment, and his method of controlling hæmorrhage. Regarding the first two points—surgical cleanliness and wound treatment—he may be said to have developed a rational asepsis. Not only did he advise that the surgeon be soberly dressed, but he mentioned the necessity for cleanliness of the hands—"Have the leech also clean hands and well shaped nails and cleansed from all blackness and filth."

His instructions about the treatment of wounds are notable. It appears to have been the normal practice to promote suppuration by applying a corrosive powder to all wounds. Arderne gives numerous prescriptions for such powders, and doubtless used them, but where he was wise in his day and generation, he insists that once such a powder had been applied and presumably a scab had formed on the wound or ulcer, the dressing should remain until "it will wilfully go out". In other words he allowed healing under the scab to proceed undisturbed. What is more important he frequently eschews the use of such corrosives altogether and advises the use of simple bland dressings.

He inveighs against the frequent dressing of wounds—though his reasons for so doing may seem to us fanciful and false. None the less he had from his own observations come to the conclusion that frequent dressing was harmful and states that often he dressed his wounds only every third day. In support of his practice he quotes Hippocrates—"The wound becometh less healthy which is often redressed", and goes on, "Let a leech be content with one dressing a day, and when he seeth a wound or an ulcer well cast out its discharge and the swelling for to vanish away and the aching for to cease and the member to come again to its first habit and colour, health is at the door if the patient be well governed, i.e. if he sleep well o' nights". There surely speaks a keen clinical observer.

The very fact that Arderne invented, described and practised a cutting operation for fistula—laying the track open to the surface by clean incision—shows that he was not deterred by fear of hæmorrhage, which was the bugbear of every operating surgeon, both before and after him. His method of controlling the bleeding from his operative incision was simple and cleanly. He did so first by sponge pressure, repeatedly applied by the surgeon, and then in the case of a fistula operation the patient was made "to sit hard on a convenient place on the aforesaid sponge"; and later, "when you deem it time" the sponge is removed, the wound sprinkled with a powder and "clean and small stupes of well teased cotton with linen clouts put on above" and the whole kept in place with a well-applied T-bandage. Many other methods for the control of hæmorrhage are described. In the lengthy section on hæmorrhoids, Arderne discusses numerous remedies—the application of cold, the use of various styptics locally applied of which his favourite was the burnt hairs of a hare, and even the use of acupressure, "sometimes it behoves for to bind the ends of the vein with a needle put under the vein, and after for to bind with a thread above the needle".

## Arderne as a Proctologist

We acclaim Arderne as the Father of British Proctology for the following reasons. Firstly—and it is for this he is best known—he described and practised what is virtually the modern operative treatment for fistula-in-ano. He himself claims that the treatment of fistula-in-ano had fallen into disrepute because it was a troublesome condition which brought little credit to surgeons, although it required long and patient treatment. The writings of his predecessors bear out these claims. Albucasis (d. 1106) taught that complete fistulæ were incurable and that all operations and the applications of ointments were but a labour in vain. Nevertheless, he suggested that laying open the fistula might be tried, though he was obviously afraid of the bleeding and advised the use of the cautery rather than the knife. He also described the treatment by the use of a thread passed through the fistula track and tied tightly, and retied till it cut its way out. De Salicet (fl. 1245), considered the most skilful surgeon of his age, wrote: "When the fistula is complete it is assuredly so difficult to cure that it is better and more honourable for the surgeon to give up the case at once." Should he undertake the case he is advised that the track should be dilated with a sponge tent and the whole track burnt with the actual cautery, or alternatively that a thread be passed through the track and daily pulled to and fro like a saw till it cut its way out—which must have been a distinctly unpleasant experience for the patient. Again Lanfranc (d. 1315) contented himself with saying that fistulæ were incurable while de Mondeville merely enlarged the orifice of the fistula with a tent and condemned those who would operate and afterwards apply a corrosive.

In contrast to all these, Arderne laid the fistula open with the knife and was confident of success. He opens his dissertation on fistula with a long list of patients whom he had cured of the disease: knights and priests, merchants and friars; he gives glory to God for his success but claims some credit also for his own hard work—"I have travailed full busily and pertinaceously". While not claiming that he could cure all fistulæ, for some he admitted were incurable, he maintains that he had mastered the problem, and, fearing to hide his light under a bushel, proceeds to describe his method in great detail. It is sad to reflect that this excellent operation of Arderne did not then become established as the treatment of fistula. For some hundreds of years after him, surgeons continued to use tents and escharotics and the cautery, and to fret the fistula with threads. So far as I can discover, these methods remained the standard practice till Percival Pott, in his monograph on fistula written in 1765, once again strongly advocated laying open the fistulous track by simple incision, and condemned the other methods of treatment to which I have referred, as well as the operation of excision of the fistulous track and the overlying tissues, which was then being practised.

Arderne is sound on all aspects of the subject of fistula-in-ano. His description of the ætiology and pathology is excellent. He accurately describes the clinical features of ischio-rectal abscess—"aposteme in the lure"—and states that such an abscess should not be left to burst but should be opened as soon as it shows softening. If it burst into the bowel, forming a so-called blind internal fistula, it was "hard of cure". If it burst both within and without it formed a fistula-in-ano, or again if the abscess had not healed in three to four months it was turned into a fistula. Furthermore he states that if the abscess opens into the rectum it is incurable.

With regard to diagnosis, he advises digital examination of the anal canal and rectum and the use of a flexible probe—the *sequere me* (follow me) he called it—to demonstrate the fistulous track. He recognizes that there is usually only one opening into the bowel, and describes cases with many openings in both buttocks, the tracks of all of which communicate with the main track (Fig. 4).

FIG. 4.—This patient is described as having a fistula-in-ano with three openings in the left buttock and three in the cleft of the scrotum. He had previously been treated by twenty doctors and had had ten operations, and was cured by Arderne in less than twelve weeks. (Reproduced by kind permission of Staples Press Limited.)

He gives advice on the selection of patients for operation and on the stage of the disease at which operation should be undertaken, namely when all inflammation has subsided. There are instructions about the pre-operative preparation of the patient, the choice of room for the operation, the position of the patient for the operation—on one side or the other according to the site of the fistula or "If the holes of the fistula be toward the rigebone (coccyx) lie he then wide open, both his legs, . . . and be they hung up with a cord or towel fastened above to a balk or beam"—which is obviously the lithotomy position. Even the position and duties of the leech's mate are described. He is to sit on the bed at the back of the patient in the lateral position and hold fast with his hands the upper buttock, raising it upward so that the surgeon may have a good view of the field of operation.

Arderne describes fully his instruments—each of which has its own name, some of them fanciful like the *sequere me*—and their exact use, and accompanying drawings give us an idea of their some-

what cumbersome shape and size (Fig. 5). His technique was perhaps unnecessarily complicated for he advises that a thread be passed through the fistulous track and tightened and then a grooved director similarly passed to guide the knife. The use of the thread seems to have been unnecessary, but from his description one gathers that he sometimes used the thread method alone without cutting at all, though he preferred a clean incision if he thought the case suitable for it. On the other hand, it may be that he could not quite break with this traditional and accepted method of dealing with the fistula.

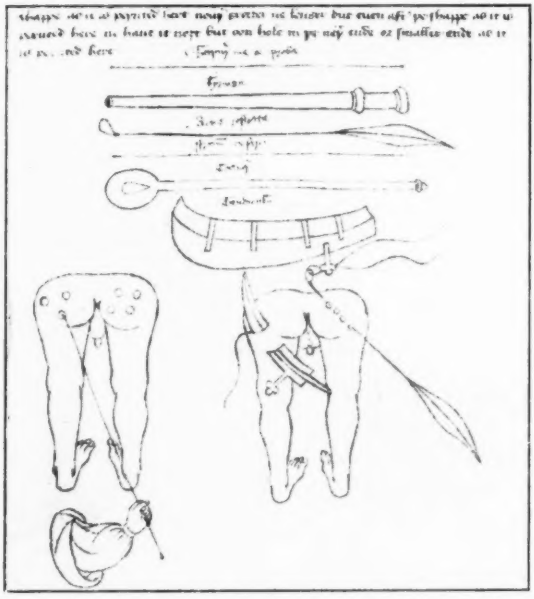

FIG. 5.—John of Arderne's instruments for fistula. (Reproduced by kind permission of *St. Bartholomew's Hospital Journal*.)

His description of the operation is very detailed—an unusual feature for a mediæval surgical treatise. After dealing with the main track, he advises that the subsidiary tracks be laid open, or if need be (presumably depending on how the patient is standing up to the ordeal), this part of the operation can be deferred till another time. Here he shows his surgical wisdom—he knows when to stop—and moreover he truly remarks that, provided the main track has been dealt with, the others may heal without further cutting.

Following the cutting, "then it is to labour to the staunching of the blood", which he did as I have already described.

The post-operative treatment is described as minutely. Simple applications—the yolk of a raw egg or common oil or oil of roses for the early post-operative period, and after eight or nine days his own powder—"pulvis sine pare". Simple enemata, administered through a clyster pipe—which he describes—are used after forty-eight hours to empty the bowel, and instructions are given as to the cleansing and drying of the wound after a motion. And so on till the twenty-fourth to twenty-eighth day, and until the healing process is complete.

Thus we are given a fascinating account of this fourteenth century surgeon's operating methods. From his descriptions there is no doubt that he dealt with severe and complicated cases—probably much more severe than we are accustomed to see to-day—and there is little doubt that he achieved considerable success in these difficult cases by using a method of operating and, what was equally important, a routine of after-care, which were far in advance of those of his contemporaries and approximated remarkably closely to our present-day methods.

While the main theme of this particular treatise of Arderne is fistula-in-ano, he also deals fully with most of the other ano-rectal conditions which we to-day have to treat. Thus he has a long dissertation on hæmorrhoids, an excellent description of cancer of the rectum, and shorter sections

on proctitis and ulceration of the rectum, prolapse of the rectum, pruritus ani and tenesmus. Furthermore he writes fully on clysters (enemata) and describes his own modification of the clyster pipe or tube, and the method of curing and preparing a pig's or neat's bladder to be attached to the clyster pipe to enable the leech to inject the enema into the bowel (Fig. 6). Time does not permit me to deal at all adequately with Arderne's writing on all these subjects, but I would like to indicate briefly some of the merits of this part of his work.

In his description of carcinoma of the rectum he brings out the features of the disease in exactly the same way as most of us would do to-day in a clinic on a patient with this condition. He explains that the tumour is hidden from sight and can be diagnosed only by digital examination, which will reveal "ane hard thing as a stone", sometimes on one side only, sometimes on both, or often involving the whole circumference, and causing great narrowing of the bowel. In the later stages it may ulcerate externally destroying the anal canal, and he gives a graphic description of such a case with total

FIG. 6.—The upper figure represents a patient with a "botch of the anus", the lower a clyster pipe with bladder attached. (Reproduced by kind permission of Staples Press Limited.)

FIG. 7.—A case of prolapsed hæmorrhoids or rectal polyp. (Reproduced by kind permission of Staples Press Limited.)

incontinence. He describes the frequent calls to stool characteristic of the disease, and the passage of fæces "medled with watery blood and stinking". He points out how often in this disease the diagnosis of dysentery is wrongly made and gives a differential diagnosis, stressing in particular that in dysentery examination with the finger will discover no abnormality in the rectum. He insists that carcinoma of the rectum is incurable and that only palliative treatment should be used. He advises the leech to warn the patient's friends that a fatal outcome is to be expected. Finally he describes the terminal stages of the disease. The whole picture is so accurately drawn that one cannot but feel that here is an observant surgeon speaking from great personal experience.

The treatise on hæmorrhoids is lengthy and perhaps chiefly remarkable for his definition and recognition of the different kinds of hæmorrhoids, of their complications and of other ano-rectal conditions which simulate hæmorrhoids. Thus he recognizes that bleeding piles are often concealed, that is, internal piles. External piles do not bleed—"there runneth nothing out of them"—and are called "deaf piles". He describes what I take to be thrombosed piles, condylomata and verrucæ

and one passage seems to deal with a prolapsed rectal polyp (Fig. 7). In contrast with his views on fistula, the views he expresses about the ætiology and pathology of hæmorrhoids are distinctly mediæval, attributing them as he does to disturbances of the humours of the body, choler and melancholy, while some references to anatomical points reveal that his knowledge of anatomy was minimal like that of all his contemporaries and of many of his successors. Nevertheless, he points out that bleeding piles are common in plethoric subjects who eat and drink too much and he advises phlebotomy in such cases. For local treatment he gives a host of remedies, recommends the use of enemata, of fomentations for inflamed piles and incision for thrombosed piles—the latter treatment, by the way, to be kept secret lest the barbers get to know of it, to the detriment of the Master Surgeons!

Tenesmus is well described—"a sickness within the bowel that maketh the patient for to desire purging of his womb . . . , for it seemeth to him continually that he must have an evacuation, and when he cometh to the privy he may not have evacuation". He gives as causes, piles, purgatives, ulceration and fæcal impaction, and as treatment his chief remedies are hot baths and enemata.

Pruritus ani is briefly referred to as "a grievous and insufferable itching in the lure", for the treatment of which he gives various remedies, one of which he refers to as "a noble ointment"! Prolapse of the rectum is described as a "going out of the lure" and for its treatment Arderne advises the local application of a host of herbal remedies, the reduction of the prolapse and the application of a firm dressing. Amongst the many local applications advised is the unguentum apostolorum—so called because it has twelve ingredients—polypharmacy with a vengeance but nevertheless, according to our author, "with this medicine was King Henry of England cured of the going out of the lure".

I have tried to paint a picture of John Arderne as a surgeon and especially as a proctologist, but the picture is unbalanced and incomplete. In my endeavour to show that he was a fine surgeon, in many ways in advance of his time, I have perhaps omitted to make clear that he was also *of* his time. He was mediæval in his love of charms and in his care to perform an operation only in the appropriate phase of the moon, for as he says, "A surgeon ought not to cut or burn in any member of a man's body, nor do phlebotomy while the moon is in a sign governing or tokening that member". He indulged in the use and was expert in the preparation of concoctions both for internal and external application—ointments, plasters, pills, confections and valences, so much so that, as I have already said, his reputation as a pharmacist excelled his reputation as a surgeon. Nevertheless, I believe we do well to honour his memory as the first great operating surgeon in England whose writings are still extant, the first of a great line of surgeons, for among his successors as surgeons and surgical writers we may count such men as Gale and Clowes in the time of the Tudors, Peter Lowe of Glasgow, the author of the "Whole Course of Chirurgerie", Wiseman the Surgeon of the Commonwealth, the great eighteenth-century figures Percival Pott, John Hunter and Astley Cooper, and, to mention only one name of the nineteenth century, the incomparable Lister. Like them, as D'Arcy Power says, Arderne learnt by experiment rather than by authority—he preferred personal experience to the teaching of the schools, which was often divorced from experience, and with characteristic frankness he related his failures as well as his successes.

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# Section of Pathology

President—Professor G. PAYLING WRIGHT, D.M., F.R.C.P.

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## DISCUSSION ON THE APPLICATIONS OF HISTOCHEMICAL METHODS TO PATHOLOGY

Dr. A. G. Everson Pearse (Department of Pathology, Postgraduate Medical School, London):

*The Meaning of Histochemistry and Some Examples of Its Application*

I shall attempt to illustrate only four facets of applied histochemistry: (1) the mucins, (2) the keratins, (3) the lipid pigments, and (4) a few examples of enzyme histochemistry.

The simple recognition of the mucins has been made much easier by the PAS reaction, which stains the majority brilliantly, and the recognition of isolated mucous carcinoma cells in smears of ascitic or pleural fluids is one of the main pathological uses of the method. These cells must be distinguished from macrophages which usually contain PAS-positive lipids. It is an alarming exercise to plot the spread of a mucous carcinoma far beyond its expected boundaries by means of this method. Applied to human and to most animal pituitary glands, with suitable counterstains, the PAS reaction provides a good method of assessing the functional state of the cells responsible for secreting the mucoprotein hormones (Pearse, 1950, 1952*a* and *b*, 1953*a*). The PAS method can also be used to trace the absorption of a foreign substance such as, for instance, tuberculous lipopolysaccharide injected into a guinea-pig or other animal. It is infuriating that this lipopolysaccharide cannot be demonstrated in the intact bacillus by the PAS method or by any other histochemical method at the present time.

A new and promising method for mucins, originated by Steedman (1950), depends on the use of a phthalocyanin dye, Alcian blue. Although excellent for epithelial mucins it is better still for connective tissue mucins. With a strong neutral red counterstain these show up very clearly and the result is particularly easy to interpret. The precise mechanism of this stain requires to be worked out. As far as I can tell it reveals only sulphate or carboxyl groups in formalin-fixed paraffin-embedded tissues. In freeze-dried tissues, however, the phosphate groups of DNA in the nuclei bind it very strongly. Nevertheless in paraffin sections with short staining times, nothing but mucin is demonstrated.

My own efforts to produce a method capable of demonstrating early keratinization in tumours have not been entirely successful. Methods depending either on selective oxidation with peracetic acid, followed by either Schiff's reagent or by dilute methylene-blue at pH 2·6 (Pearse, 1951) demonstrate keratin at about the stage where it is recognizable by histological methods alone. Methods depending on alkaline hydrolysis in the presence of tetrazolium salts (Pearse, 1953*b*) are a little better. Recently Scott (1953) has suggested that a combination of peracetic acid, followed by the aldehyde-fuchsin reagent (Gomori, 1950), is capable of demonstrating keratin with much greater selectivity. If this is so, the combined method may be a valuable one in applied histochemistry.

As an example of pure histochemical analysis one may suggest, for instance, investigations into the nature of the intestinal pseudomelanins. After a negative Perles' reaction one is left with a brownish pigment which might be lipofuscin, lipochrome, adrenochrome, melanin, or something else altogether. Schmorl's ferricyanide reaction (Lillie and Burtner, 1953) is strongly positive. This indicates reducing properties shared by melanin, lipofuscins, sulphydryls and aldehydes. Sulphydryls and aldehydes can be shown to be absent, however. The PAS reaction is positive, more so in the youngest than in the older pigment granules, indicating carbohydrate or unsaturated lipid; a positive peracetic acid—Schiff reaction indicates preferentially the latter. The alkaline tetrazolium reaction gives an alcohol-soluble formazan dye, indicating lipofuscin rather than carbohydrate and excluding melanin altogether. The fact that the granules fail to bind methylene-blue, from dilute solutions, below pH 3·6 also excludes the true melanins. Strong autofluorescence supports the idea of an unsaturated lipofuscin. Only one reaction suggests anything further. This is the diazonium reaction in alkaline solution. The production of a red colour in this case indicates the presence of a phenolic factor. Probably phenolic oxidation products from the gut combine with the young lipofuscin, tanning it as do the phenols in the insect cuticle. These phenols may certainly be derived, as an old and recently revived theory (Speare, 1951) maintains, from intemperate addiction to *cascara sagrada*.

This purgative contains anthracene glucuronides, *inter alia*. An enormous number of tissue components await simple analytical histochemistry of this kind but, unfortunately, it is seldom possible to obtain accurate information without recourse to a relatively large number of independent reactions.

Turning now from analytical to functional problems I should like to end with some examples of enzyme histochemistry. There are modern techniques for localizing at least 20 different enzymes but the majority of these are accurate only on the histological scale. That is to say they will distinguish between one cell and its neighbour but they will not localize the enzyme accurately within the cell itself. The importance of histochemical, as opposed to purely biochemical, methods is that even the relatively crude ones can localize enzymes in a way which is not possible by any other means. Cessation of function, hydrolytic or oxidative, can speedily be demonstrated even if it affects only one cell in a hundred in a given tissue. Alterations of function can similarly be detected. At present the interpretation of such alterations is not easy and it will only be simplified when the techniques are in widespread application to normal and diseased tissues.

Relatively simple coupling azo dye methods exist for alkaline and acid phosphatases, and for non-specific esterases. If these are applied to formalin-fixed frozen sections the accuracy of localization is sufficient for histological purposes. Localization of enzymes within the cell can be achieved by some of the older enzyme methods, if particular care is taken in incubation, and by the substituted indoxyl methods (Holt, 1952; Holt and Withers, 1952) for esterases, cholinesterases and phosphatases. When these become available for general use, and when indoxyl substrates have been prepared which will cover a wide spectrum of enzymes, we shall be able to detect alterations in cell function by relatively minute intracellular alterations in enzyme concentration or localization.

At present two methods, both capable only of localization on the histological level, are especially useful for application to histopathological problems. These are the coupling azo dye method for esterase (Pearse, 1953*c*) and the neotetrazolium or blue tetrazolium method for succinic dehydrogenase (Rutenburg *et al.*, 1953). Less useful generally, but applicable to a number of special problems, nevertheless, are the coupling azo dye methods for alkaline phosphatase (Gomori, 1951) and for acid phosphatase (Grogg and Pearse, 1952). Only one of five available methods for β-glucuronidase (that of Friedenwald and Becker, 1948; modified by Burton and Pearse, 1952) is worthy of application to pathology. It is a tedious method, however, requiring a considerable amount of patience in practice.

It is not possible, in a short communication such as this, to present more than a fraction of the histochemical methods worthy of application to pathological problems. I believe that difficulties in interpretation of many of the methods and the fact that they will probably be succeeded in the future by better and more accurate methods, should not prevent their present use in histological and other routine laboratories. They may not provide, at once, the answer to any particular problem: probably they will not do so. They can be relied upon, however, to provide an abundance of new questions and ideas and out of these, and from attempts to solve them, may come the answer which is sought so urgently.

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**Professor J. F. Danielli** (Zoology Department, University of London King's College):

### *Cytochemistry in Pathology*

There are two broad fields of cytochemistry, namely, the use of cytochemical methods in the investigation of disease by laboratory methods, and the use of cytochemistry for diagnosis and clinical studies.

*The investigation of disease.*—In so far as the chemical aspect of a lesion or disorder is worthy of study, cytochemistry is the method of choice, if good techniques are available. But in my opinion, it is necessary to adopt a much more critical attitude towards cytochemical techniques than has been common practice in recent years. I have recently published a detailed analysis of certain cytochemical techniques (Danielli, 1953) and a series of critical reviews by other authors are appearing in the *International Review of Cytology*. What can be said here must be regarded as a very limited survey of what appears in these reviews.

The majority of cytochemical methods fall into one of two groups: The first consists of end-group methods, in which a chemical grouping present in molecules such as those of polysaccharides, nucleic acids and proteins is caused to react with an appropriate chemical reagent so as to produce a change in the absorption spectrum of the specimen. Perhaps the best-known example of this technique is Feulgen's use of reduced fuchsin to indicate the presence of aldehyde groups. The second group consists of methods whereby an enzyme is allowed to act upon a soluble substrate, producing a substance which is precipitated near the site of enzyme action. The best known of these methods is the calcium phosphate precipitation test for alkaline phosphatase, originally introduced as a histochemical method by Robison and elaborated into a cytochemical method by Gomori and Takamatsu.

The most common errors which are encountered in techniques of these two types are as follows:

(*a*) *Fixation artefacts.*—Fixation by chemical reagents is always liable to produce artefacts of considerable magnitude and is now well known to produce large artefacts, particularly in the distribution of glycogen and pentose nucleic acid in cells. In view of this difficulty, it is unwise to use any method other than freeze-drying if the precise localization of chemical substances has to be investigated.

(*b*) *Diffusion artefacts.*—Diffusion artefacts may arise both by the diffusion within a cell of the substance under investigation, by diffusion of the end products of a cytochemical reaction and by failure of substrates to reach enzymes which are protected by membranes, &c. These artefacts can only be controlled on a cytological level by careful and detailed investigation.

(*c*) *Chemical errors.*—Very few, if any, of the cytochemical agents which are available are absolutely specific. In view of this, it is always necessary, if completely reliable identification of a substance is required, to use a variety of cytochemical methods for the examination of each cytochemical entity.

(*d*) In quantitative studies errors due to scattering of light in the specimen and heterogeneous distribution of substances within the specimen must be carefully evaluated.

It is clear from this list of possible errors that a cytochemical investigation is likely to be hazardous unless it is conducted by a team containing individuals trained in the relevant biological sciences, in chemistry and in physics.

*Clinical Studies and Diagnosis.* Such cytochemical methods as are reliable and reasonably simple will turn out, one can believe, to be of considerable value under clinical conditions. But in addition to this, it may well prove useful to use other simple methods which, whilst not permitting the precise cytochemical localization of a substance and perhaps not always permitting a precise chemical interpretation, may nevertheless be rapid and reproducible. Such methods have a potentiality of adding considerably to the repertoire of techniques which the pathologist finds useful in diagnosis. In certain circumstances also, such techniques may be of considerable value in the orientation of treatment. For example, it is likely that in the future enzyme-activated drugs will come into use for the treatment of cancer. The examination of tumour biopsies by cytochemical methods will probably be the only practical method of finding which enzymes are present in the tumour under consideration, and thus these methods will be decisive in deciding which drugs may be employed. For a purpose such as this, it is not necessary to have a precise cytochemical technique: all that is required is a technique which is capable of demonstrating in a semi-quantitative manner the presence of an enzyme on the histological level.

To sum up, it seems likely that, provided a sufficiently critical attitude is adopted towards cytochemical techniques, these techniques will prove of value in fundamental studies of the chemical aspects of diseases, and some histochemical techniques at least will prove of some value in the hands of the clinical pathologist.

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**Dr. G. H. Bourne** (Histology Department, London Hospital Medical College):

*Some Histochemical Techniques of Possible Value to Pathology*

There are two groups of techniques which may be of interest to pathologists. The first of these is that used for the demonstration of phosphatases and was developed by Gomori (1951) and the second is one in which the substrate used is dehydrogenated by the enzyme concerned (a dehydrogenase) and the liberated hydrogen reduces tetrazolium, producing an insoluble diformazan at the site of enzyme activity (Rutenburg, Gofstein and Seligman, 1950).

The use of the phosphatase technique to demonstrate the localization of non-specific alkaline phosphatase is well known. In this technique the substrate used is glycerophosphate. If various sugar phosphates (i.e. those of glucose, galactose and fructose) are used as substrates instead of glycerophosphate it can be seen that they are apparently dephosphorylated by non-specific phosphatase. However, not all phosphate esters seem to be hydrolysed by this enzyme or complex of enzymes. Two esters which are themselves prosthetic groups of enzymes (pyridoxal phosphate and riboflavin 5′-phosphate) appear to be dephosphorylated at an alkaline pH by enzymes which are different from the non-specific phosphatase and different from each other. The difference between the reactions given with these two substrates and glycerophosphate is well demonstrated in heart muscle. With glycerophosphate there is a very strong reaction by all the capillaries and also by the intercalated discs of the heart muscle fibres. With riboflavin phosphate the discs are positive and so are the nuclei of the endothelial cells of the capillaries, with pyridoxal phosphate the capillaries are completely negative and the sarcosomes very positive. The intercalated discs are not distinguishable. It is possible that the regions of localization of enzymes which dephosphorylate riboflavin phosphate and pyridoxal phosphate may actually indicate sites of synthesis of these phosphates and that under the conditions of the histochemical reaction the synthetic enzymes are behaving hydrolytically.

Other phosphate substrates which have been investigated are those of œstrone, stilbœstrol and hexœstrol. There is no particular evidence that phosphorylation and dephosphorylation play a part in the normal metabolism of sex hormones but it is of interest that these phosphates, too, are hydrolysed by enzymes which differ, at least in distribution, from non-specific phosphatase and from those which split the two vitamin phosphates already mentioned. It is of interest, too, that (again based on distribution) the stilbœstrol and hexœstrol phosphates are dephosphorylated by the same enzyme, but that which splits œstrone phosphate is different. This is well shown in the jejunum where the brush border of the epithelial cells and all the nuclei in the section give a strong positive reaction with the first two sterol phosphates, the Golgi apparatus being negative. With œstrone phosphate on the other hand, the brush borders are completely negative but the nuclei and Golgi apparatus of the epithelial cells and most of the other nuclei in the section are also positive. Differences from non-specific phosphatase were also found in other organs, e.g. kidney, brain, adrenal and testis.

The second type of technique has been used to demonstrate two enzymes or enzyme systems. The first of these is succinic dehydrogenase and the second is xanthine oxidase. The latter of these two techniques in particular may ultimately prove of great interest to experimental pathologists but it is not yet in a state in which it can be used experimentally. The reaction is erratic and the phosphate buffer, which biochemically seems to be the most suitable for use with this method causes swelling and gelatinization of the tissues making them very difficult to handle. The succinic dehydrogenase complex can, however, be demonstrated with regularity in tissues and the activity of this enzyme in a number of organs has been found to be increased by the injection of cortisone. This is found to be the case, for example, in heart muscle. But although the activity of the heart muscle fibres is increased by cortisone that of the intercalated discs is rendered inactive. It is possible that this is a normal "stress" reaction of heart muscle since it has also been found in the heart of a human dying under considerable stress. This reaction by the intercalated discs and the presence in them of dephosphorylating enzymes suggest that they play a very important part in the physiology of heart muscle. It has been suggested by the present author (Bourne, 1953) that they are concerned with the "boosting" of the contraction wave along the fibre.

The examples given show how certain histochemical techniques can be used in research into the normal functioning of organs and they may equally well be used to supply information in the study of abnormal function.

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**Dr. K. W. W. H. Walton** (Department of Experimental Pathology, University of Birmingham):

*Histochemical Investigation of the Polymerization of Acidic and Neutral Polysaccharides*

The mucopolysaccharide constituents of the connective tissues are thought to undergo structural alterations in various disease processes. There has been much conjecture about the significance of

the accompanying alterations of certain staining reactions applied to these tissues. For instance, it has been suggested that the intensity of metachromasia may be an index of the degree of polymerization of acidic polysaccharide components and that alterations in the intensity of staining with the Periodic Acid Schiff (PAS) technique may indicate altered polymerization of neutral polysaccharide components (Gersh, 1951; Loewi, 1953).

*In vitro* studies were undertaken to investigate these questions.

*Acidic polysaccharides and metachromasia.*—If the concentration of a dilute solution of toluidine blue is kept constant and increasing amounts of an acidic polysaccharide, such as heparin, are added, the colour of the solution changes from blue through purple to reddish-violet. It has been suggested by Michaelis (1947) that these changes occur because the basic groups of the dye molecules form salt-linkages with the acidic (sulphate) groups of the polysaccharide. Dye molecules thereby are brought into close proximity with one another allowing loose association to occur by van der Waal's forces between adjacent dye molecules and thus effectual polymerization of the dye.

The acid polysaccharide-dye complex is less soluble than the dye itself. It has been shown by MacIntosh (1941) that if the mixture is shaken with petroleum ether the metachromatic or bound component separates as a layer at the interface leaving the unbound dye in solution. The difference between the optical density of the dye left in solution and that of the original is thus a measure of the amount of dye bound in the metachromatic complex.

Using MacIntosh's method, experiments were designed to investigate whether the amount of dye bound metachromatically was influenced by the number and nature of the acidic groups of the polysaccharide or by the extent of its polymerization.

In the initial experiments, sulphate esters of glucose polymers were employed. These varied in size from glucose sulphate to a dextran sulphate containing about 6,000 glucose-units. The compounds were found to give a linear relation between sulphate content and metachromatic activity. But no relation was demonstrable between metachromasia and the extent of their polymerization.

Another experiment indicated that not only the number, but also the *nature* of the acidic groups influenced metachromatic activity. Glycolic ethers of methyl glycosides of different dextrans were prepared and their activities contrasted. It was found that these carboxylated polysaccharides also showed some activity but that concentrations several hundred times greater than those of the corresponding sulphated compounds were necessary to give the same degree of metachromasia.

Other authors have shown that polyphosphates (Wiame, 1947; Weissman, *et al.*, 1952) and silicates (Merrill, *et al.*, 1948) may also be metachromatic.

On comparing the metachromatic activity of miscellaneous synthetic and naturally occurring polysaccharide sulphates (sulphate esters of polyuronic acids, polyamino-sugars, chondroitin sulphate, heparin, &c.) with that of the dextran sulphates it was found that once again activity could be correlated with sulphate content, regardless of the nature of the parent polysaccharide.

From these experiments it was concluded that the metachromatic activity of acidic polysaccharides is determined by the number and nature of their acidic groups and not by the degree of polymerization nor by the nature of the component saccharide units.

*Neutral polysaccharides and the PAS reaction.*—On the other hand, on oxidising dextrans of different degrees of polymerization with periodic acid and then exposing them to the Schiff reagent it was found that the depth of colour produced *decreased* with successive depolymerization. This is not in keeping with the hypothesis of Gersh (1951) who suggested that *increase* in the intensity of PAS staining of the ground substance of connective tissues and basement membranes might connote depolymerization of the polysaccharide component. At the moment, no satisfactory chemical explanation can be advanced to explain the present finding but it appears to confirm the observations of Pearse (1953) upon the PAS staining of other polyglucosides.

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# Section of Odontology

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[*November* 23, 1953]

## The Growth of the Human Face

By JAMES H. SCOTT, M.D.

(*Department of Anatomy, The Queen's University of Belfast*)

### INTRODUCTION

THE growth of the human face presents some of the most complex problems of biology, problems which continue to attract the attention of many anatomists and dental research workers. It is not intended in this paper to deal with all the data, experimental and clinical, which has accumulated but rather to attempt the construction of an hypothesis adequate to correlate some of the accumulated information.

### GENERAL PRINCIPLES OF SKELETAL AND CRANIAL GROWTH

Growth of the individual elements of the skeleton takes place in one of two ways. (1) The deposition of bone on the surface of cartilage beneath a perichondrium which is becoming a periosteum, followed by the deposition of new bone on the surface of the older bone (surface accretion). In some cases (membrane bones) the earliest bone is laid down in an area of mesodermal condensation in which there is no cartilage. (2) The replacement of growing cartilage by bone (endochondral ossification). In long bones growth in width is produced by surface accretion and growth in length by endochondral ossification at the epiphysis.

There is also a process of internal reconstruction involving the cortical and trabecular structure of individual bones whereby they can continually adapt their internal structure, and to a more limited extent their external form, to the changing requirements of function.

Growth by the replacement of cartilage by bone is an important factor in the growth of the cranial base (which forms the junctional region between the face and cranium), in the condyles of the mandible, and in parts of the facial skeleton related to the nasal capsule. Growth of cartilage continues at some of these sites throughout childhood to the threshold of adult life. It can be stated as a generalization that the growth of cartilage is most active during late fœtal life and early childhood and thereafter becomes of less importance. Co-ordinated bone deposition and resorption is the method whereby the facial and cranial elements increase in size, alter in form and become stronger. This method of growth commences at about the time of birth and becomes of greater significance as development proceeds. In later childhood it is the most important method of growth of the facial skeleton.

### Growth at Sutures

The various bony elements making up the facial skeleton begin to develop close to the primordial facial skeleton comprising the cartilage of the nasal capsule and Meckel's cartilage (Fig. 1). The centres of ossification of some of these bony elements are also related to important nerve trunks (e.g. the mandible, maxillæ and palatine bones). Some develop in membrane just outside the perichondrium of the primordial cartilaginous skeleton; some replace part of the cartilaginous skeleton (ethmoid, inferior turbinate); some in their further growth are associated with masses of secondary cartilage (mandible, maxilla). All of them, however, are at first widely separated from one another and each developing element is enclosed within its own periosteal capsule consisting of an inner

Fig. 1.—Coronal section of the face of a 70 mm. C.R. human fœtus showing Meckel's cartilage, the cartilage of the nasal capsule and the related bones; the mandible, maxilla, zygomatic and vomer.

cellular osteogenetic zone and an outer fibrous membranous part. The periosteal capsules contain at an early stage all the bone-forming cells from which, and from the descendants of which, the bony element is derived. It is unlikely that at a later stage there is any migration of bone-forming cells from outside the periosteal capsule. Therefore the intracapsular osteogenetic cells by their activity and the pattern of their mitotic divisions determine the form of the bony element which is derived from them. They are in all probability the gene-controlled determiners of bone morphology. As they grow, the separate bony elements approach one another until there is a stage in which there is contact between the outer membranous layers of their periosteal capsules, each developing "suture" showing four zones between the actual bony elements (Fig. 2). These are the cellular and membranous regions of the periosteum of each skeletal element. This stage is followed by a union of the membranous layers producing a condition in which there are three zones at each suture. By the union of the adjacent membranous layers at a developing suture, the suture becomes both a site of growth (by surface deposition resulting from the activity of the cellular layers which remain distinct for each bony element) and a site of union. Later, the collagenous fibre bundles become reorientated and run directly from one bony element to the other. The bone-forming cells (osteoblasts) are then greatly reduced in number and are concerned chiefly in the process of internal reconstruction related to the stresses acting upon the bony elements.

The bony elements are not thrust apart by the new bone formed at the sutures as is sometimes taught. Growth takes place at the suture surfaces of the bones by surface deposition as the bony elements are being separated by the growth of cartilage, and by the expansion of organs such as the brain and eyeballs. Sometimes cartilage is present at the sutures themselves as in the mid-palatal suture of such animals as the rat, cat and wallaby. In the growth of the face the cartilage of the nasal capsule, and especially the cartilage of the nasal septum, is an important factor in separating the bony elements which have developed round it and may be regarded as a pacemaker for facial growth. This power of cartilage to separate growing bones at sutures resides in its method of interstitial growth, its turgidity and its ability to resist deforming forces. When bones are no longer

being separated at their sutures, growth ceases there except for the overlap of one bony element upon another as along the margin of the squamosal part of the temporal bone. Adjustments to alternating stresses upon the bony elements in contact at a suture line, which produce the zigzag type

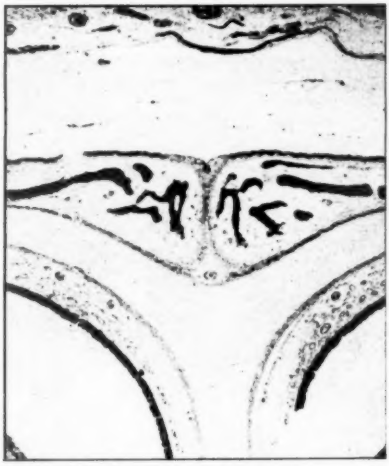

FIG. 2.—Coronal section of a 125 mm. C.R. sheep fœtus showing the suture between the nasal bones with the four primary layers of the sutural tissue. In the upper part of the suture the membranous layers are uniting.

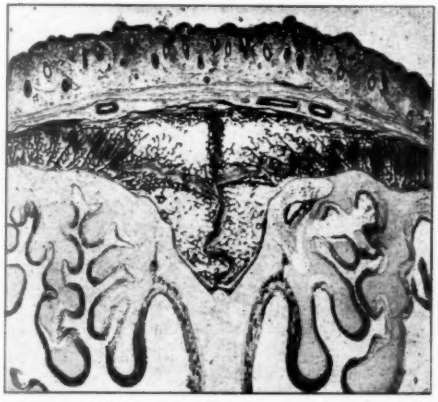

FIG. 3.—Coronal section of a newborn pig showing the zig-zag suture formation at the fronto-nasal region.

of suture (Fig. 3) should be regarded as internal reconstruction rather than true growth. Madder or alizarin, however, would fail to distinguish between the bone deposited in a reconstruction as opposed to a process of expansion.

## SITES OF SKELETAL GROWTH IN THE SKULL

*The Cranial Base.*—This region is of importance because it is the junctional area between the cranial and facial parts of the skull and because it is used, or parts of it are used, in many of the superimposition techniques in the analysis of skull growth. In man, after birth, it consists of four elements between basion and nasion; these are the basi-occipital, the sphenoid (presphenoid and basisphenoid unite just before birth), the cribriform plate region of the ethmoid (mesethmoid), and the frontal. It can be divided into three parts for the purpose of analysing its growth (Fig. 4).

(1) From basion to the anterior margin of the pituitary fossa. This posterior section grows chiefly by the proliferation of cartilage at the spheno-occipital synchondrosis.

(2) From the anterior margin of the pituitary fossa to the foramen cæcum. This intermediate part grows at the spheno-ethmoidal suture which continues outwards on the roof of each orbital cavity as the spheno-frontal suture.

(3) From the foramen cæcum to nasion. This anterior segment grows by deposition on the anterior surface of the frontal bone and is related to the degree of development of the frontal air sinuses.

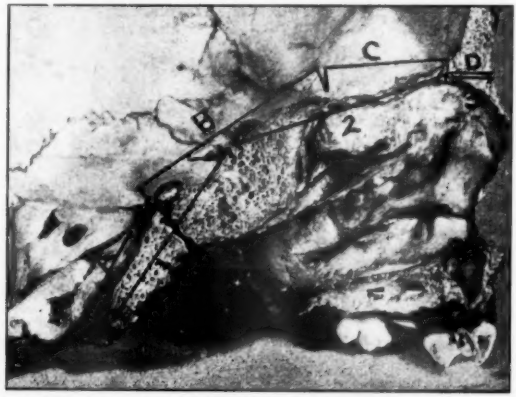


FIG. 4.—Cranial base of a child of 4 years of age to show its form and structure. A, basi-occipital. B, body of sphenoid. C, cribriform plate of ethmoid. D, frontal. 1, 2, 3 are the three parts used in growth analysis.

After the seventh year, growth is completed in the middle segment: that is, there is little if any further growth at the spheno-ethmoidal and spheno-frontal sutures (*see also* de Coster, 1951). Growth continues at the basi-occipital synchondrosis and at the surface of the frontal bone until the end of the second decade. Hence, while growth of the cranial base continues throughout childhood and adolescence it does not occur in all its parts to the same extent.

*The coronal suture system.*—Growth of the cranial vault in the antero-posterior direction involves two suture systems separating three cranial regions (Fig. 5). These are (1) the lambdoidal suture

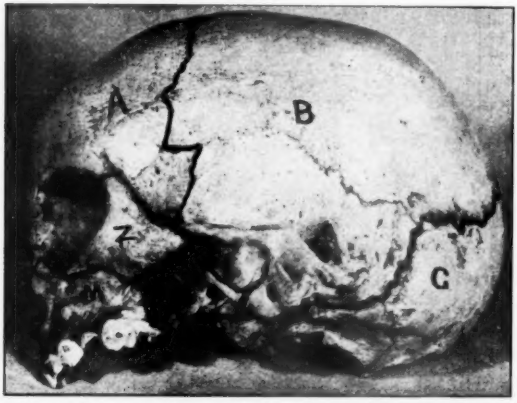


FIG. 5—Skull of a child of 4 years of age showing the cranial segments and the maxillary sutures. A, anterior cranial segment. B, middle cranial segment. C, posterior cranial segment. Z, zygomatic bone. M, maxilla.

system separating the occipital bone behind from the parietal and temporal bones in front. The occipital bone forms the posterior cranial segment and the parietal and temporal bones the middle cranial segment. (2) The coronal suture system above the pterion separates the frontal from the parietal bones. Below the pterion it divides into two parts, an anterior, running between the frontal

and great wing of the sphenoid, and a posterior running between the great wing of the sphenoid and the temporal. The posterior limb is the more important and with the supra-pterion part of the coronal suture system separates the frontal and sphenoid bones in front from the parietal and temporal bones behind. The frontal and sphenoid bones make up the anterior cranial segment and except for the zygomatic arches carry the skeleton of the upper face. At the cranial base the lambdoidal suture system and the posterior limb of the coronal suture system meet in relation to the spheno-occipital synchondrosis. This synchondrosis is therefore an important element in the growth of both these suture systems. At this synchondrosis the anterior (sphenoid) and posterior (occipital) cranial segments meet one another. The middle cranial segment does not reach to the middle line of the cranial base.

The basi-occipital synchondrosis lies in the roof of the nasopharynx and the growth of its cartilage elongates the cranial base. It also projects the whole upper facial skeleton forward from the vertebral column; increases the antero-posterior extent of the nasopharynx, and makes room for the growth of the muscles of mastication and for the growth of the mandibular ramus. Growth at the synchondrosis will also increase the size of the cranial cavity. In later childhood this increase in size is probably associated with thickening of the skull by surface deposition on the interior of the bones of the vault, rather than any growth in brain size.

Examination of a skull shows that the anterior limb of the coronal suture system separates the zygomatic bone and great wing of the sphenoid bone within each orbital cavity and at the cranial base it includes the suture between the small wing of the sphenoid and the frontal bone, and between the sphenoid and ethmoidal bones. That is, the anterior limb of the coronal suture separates the sphenoid bone and its various processes from the ethmoid, frontal, zygomatic and palatine bones. It is an important site of cranial, orbital and facial growth during late fœtal life and up to about the seventh year.

*The nasal septum.*—The nasal septum at birth consists of hyaline cartilage which is continuous above and behind with the cartilage of the cranial base. This region of the cartilaginous cranial base has been largely replaced by the body of the sphenoid bone. Below, the lower free margin of the septum is embraced for the greater part of its extent by the developing bilaminar vomer which interposes itself between the septal cartilage and the hard palate. In front, however, the cartilage reaches the maxilla (its premaxillary part) above and behind the nasal spine of the nasal aperture. The cartilage is not directly united to the vomer but lies along the vomerine groove and is separated from the bone by perichondrium and a mass of loose fatty tissue. It is more firmly united by fibrous tissue to the premaxillary region of the maxilla in front of the vomer. At the roof of the nasal cavity the cartilage of the septum is continuous with the cartilage of the side walls of the nasal capsule behind and in front of the opening for the olfactory nerves (cribriform plate region). The greater part of the cartilage of the lateral wall of the capsule is replaced by the lateral masses of the ethmoid bones in which the ethmoidal air cells develop, and by the inferior turbinate bones.

Soon after birth a centre of ossification appears in the upper back part of the cartilaginous nasal septum. This is the centre for the mesethmoid which is an element of the cranial base. Ossification from this centre extends downwards as the perpendicular plate of the ethmoid, and upwards into the crista galli to which the falx cerebri is attached. Between 3 and 5 years of age ossification extends across the cribriform plate region to unite the facial (lateral mass) and cranial (mesethmoid) elements of the ethmoid. About a year later the perpendicular plate unites in bony union with the vomer at the back of the nasal septum. After the 7th year there is no further growth of the cribriform plate (intermediate segment of the cranial base) and two of the facial bones, the lateral mass of the ethmoid and the vomer, are now united to the most anterior element of the cranial base (mesethmoid). In many animals such as the sheep, pig, and elephant, the mesethmoid is absent and the perpendicular plate of the ethmoid is formed by a forward extension of the sphenoid (presphenoid).

Growth of the cartilage of the nasal septum will thrust all the facial bones (except the mandible) downwards and forwards from the cranial base and separate them from one another (Scott, 1953). The union of the parts of the ethmoid with one another and with the vomer stabilizes the craniofacial union. Growth of the septal cartilage could still, in theory, separate the maxillary and palatine bones from the ethmoid and vomer and thus produce the deepening of the nasal cavities which occurs after the seventh year.

*The maxillary sutures.*—The most important sutures related to the maxilla from the point of view of its growth are those between the maxilla and the frontal, zygomatic, ethmoid and palatine bones. It has been pointed out (Weinmann and Sicher, 1947) that these sutures are, in general, so disposed that growth at them would thrust the maxilla downward and forward (Fig. 5). The form of the frontomaxillary suture is, in fact, so disposed, but a careful examination of the zygomatic-maxillary suture shows that growth at this suture would thrust the zygomatic bone outwards or the maxilla inwards, while the suture between the ascending process of the palatine bone and the maxilla in the lateral wall of the nasal cavity is so complex that growth at the suture could have no direct effect in moving the maxilla. These sutures are so arranged, however, especially in early childhood, as

to permit the maxilla to be thrust downward and forward between the adjacent bones by the growth of the septal cartilage and the contents of the orbital cavities.

By the seventh year growth of the orbital cavities is almost complete and any further thrusting downwards of the maxilla would continue to increase the height of each orbital cavity. This could be compensated for by deposition of bone on the orbital surface of the maxilla which would, however, be associated with an increase in height of the maxillary antrum above the level of its opening into the middle meatus. It would also convert the whole of the infra-orbital groove on the orbital floor into a canal. These changes do not, however, take place so that the deepening of the nasal cavities which occurs after the 7th year must be produced by resorption on the floor of each cavity and deposition of new bone on the oral surface of the hard palate. That this occurs is shown by the deepening of the inferior meatus and the development of the maxillary crest at the base of the nasal septum.

*The sutures of the zygomatic bone.*—Separation of the zygomatic and temporal bones at the suture of the zygomatic arch is produced by growth of the cranial base at the spheno-occipital synchondrosis. It is therefore part of the coronal suture system. The suture between the maxilla and zygomatic bones has already been described. It is part of the septal suture system in that the bones forming it are separated by growth of the cartilage of the nasal septum. It is also, however, with the suture between the zygomatic bone and great wing of the sphenoid, concerned in the growth in width of the face and especially in the growth in width of the orbital cavity. The zygomatico-frontal suture is related to the growth in height of the orbital cavity.

The zygomatic bone, therefore, is related in its growth to the eyeballs, septal cartilage and the cartilage of the cranial base. The cartilage of the cranial base is a site of growth up till the end of the second decade; the septal cartilage and eyeball have completed their growth before the end of the first decade.

It should be remembered that sutures are places where the bony elements of the skull are united to one another and the growth of such organs as brain and eyeball and of cartilage, unless there is actual bony union, will involve more than one bony element and more than one suture system. For example, up to the 7th year the septal cartilage thrusts the maxilla downwards and forwards, but because this bone is united to the zygomatic and palatine bones by sutures these bones will also be drawn downwards and forwards. Growth of the basi-occipital synchondrosis will separate the temporal and zygomatic elements of the zygomatic arch and will also tend to draw the zygomatic bone backwards with the temporal bone. It is the total result of such growth tensions which determines the amount of growth at the various sutures.

The zygomatic bone is an important element in the facial buttress system whereby the forces of mastication are transmitted from the teeth to the cranial base. With the development of the dentition there is an increase in these forces and correlated with this a reconstruction of the bony architecture involving the sutural regions. As a result madder feeding or alizarin red will indicate bone formation, which need not, however, indicate expansive bone growth.

*The lower jaw.*—Growth of the mandible has received much more attention than growth of the other bones of the face. The characteristic feature is the importance of the secondary cartilage of the head of the condyle. Growth in height of the body is mainly by deposition along the subgingival alveolar border, and growth in width of the ramus is entirely by growth at its posterior edge. It is uncertain how much growth takes place along the outer surface of the body in the human mandible. Studies in comparative anatomy indicate that in many animals growth in length of the mandible is the result of surface deposition in front as well as at the posterior borders of the rami. Recent work shows that surface deposition at the front of the mandible is a factor of some importance in the monkey (*Rhesus macaque*) (Baume, 1953). Growth in length of the mandible is closely correlated with growth in width of the ramus. If all or most of the growth takes place at the back of the ramus there must be an extensive resorption of bone at the front of the ramus to uncover the developing permanent molars. It is usually held that there is some resorption of bone in this position, but there is probably less than the amount needed to uncover the three permanent molars, as there is a good deal of evidence that the teeth migrate forwards from their developmental position in the alveolar bulb. The presence of osteoclasts along the anterior edge of the coronoid process may be associated with adjustment of the attachment of the temporal muscle in a manner similar to the changes occurring in relation to the attachment of the lateral pterygoid (Symons, 1953).

It is usually stated that growth of the condylar cartilages thrusts the mandible downward and forward from the glenoid fossæ. It may be more accurate to say that growth of the cartilage permits of growth of the condyle upwards and backwards so as to maintain contact at the temporo-mandibular joint as the mandible is carried downwards and forwards by the growth of the upper facial skeleton. The head of the condyle is very similar to the two ends of the clavicle and it is probably more accurate to state that growth of the clavicle takes place so as to maintain contact with the sternum at one end and the scapula at the other, rather than to say that growth of the clavicle thrusts the scapula away from the sternum.

### The Rate and Pattern of Facial Growth

Table I gives the measurements of some facial and cranial dimensions at birth, 3, 7, 10 years and in the adult. The measurements are mean values for male children and do not take account of the variation about the mean for each age group. The data, however, does show that at 7 years cranial length, cranial width and orbital height are nearly 95% of the adult dimension, while facial height is only 80%. At 10 years the cranial and orbital measurements have reached or exceeded 95% of the adult size, while the facial measurements have reached to about 85% of the adult size. At 10 years the height of the maxillary antrum is only 55% of the adult size. Growth in height of the antrum is closely related to growth of the maxillary alveolar process.

[Throughout this paper measurements are expressed in millilitres and millimetres.]

Table I.—Cranial and Facial Measurements (Male) at Birth, 3 Years, 7 Years, 10 Years, and in the Adult

(data from various sources)

| Measurement | Birth | 3 years | 7 years | 10 years | Adult |
|---|---|---|---|---|---|
| Cranial capacity .. .. | 350 (24%) | 1,225 (82%) | 1,350 (90%) | 1,425 (95%) | 1,500 |
| Cranial length .. .. .. | 120 (60%) | 175 (88%) | 185 (93%) | 190 (95%) | 200 |
| Cranial width .. .. .. | 95 (63%) | 135 (90%) | 142 (95%) | 145 (97%) | 150 |
| Orbital height .. .. .. | 18 (55%) | 26 (79%) | 31 (94%) | 32 (97%) | 33 |
| Cranial base .. .. .. | 56 (56%) | 76 (76%) | 85 (85%) | 90 (90%) | 100 |
| Bizygomatic width .. .. | 85 (61%) | 112 (80%) | 116 (83%) | 122 (87%) | 140 |
| Upper face height .. .. | 30 (43%) | 50 (70%) | 56 (80%) | 60 (86%) | 70 |
| Total face height .. .. | 50 (40%) | 85 (65%) | 100 (80%) | 105 (84%) | 125 |
| Height of maxillary antrum .. | 5 (18%) | 12 (36%) | 17 (51%) | 18 (55%) | 33 |

Figures in brackets give the percentage of the adult dimension.

It is interesting to note that in its growth the cranial base (basion to nasion) is intermediate between the cranial and facial dimensions. Growth of the middle segment of the cranial base, however, (pituitary fossa to foramen cæcum) is completed by the 7th year.

The well-known difference in the growth rate of the cranial and facial parts of the skull can be demonstrated by using cranial and facial modules. The cranial module is here taken as the sum of cranial length and cranial width divided by 2, and the facial module as the sum of total facial height and bizygomatic width divided by 2.

Table II gives the modules at different ages (data from Low, 1952 and Flemming, 1933).

Table II.—Cranial and Facial Modules (Male)

| | Cranial module | Facial module |
|---|---|---|
| 3 days .. .. | 108 | 69 |
| 1 year .. .. | 145 (37) | 91 (22) |
| 3 years.. .. | 156 (11) | 100 (9) |
| 5 years.. .. | 159 (3) | 105 (5) |
| 8 years.. .. | 162 (3) | 107 (2) |
| 10 years.. .. | 165 (3) | 109 (2) |
| 12 years.. .. | 166 (1) | 112 (3) |
| 15 years.. .. | 171 (5) | 121 (9) |
| 17 years.. .. | 173 (2) | 126 (5) |
| Adult .. | 175 (2) | 133 (7) |

Figures in brackets show increase over previous measurement.

It will be seen that while the cranial module increases by a little over 50% from 3 days to adult life, the facial module increases by a little less than 100%. Note that in both cranium and face the greatest amount of growth takes place in the first year; that the period of rapid post-natal growth ceases in the cranium at the end of 3 years, and in the face at the end of 5 years; that there is a slight increase in the rate of cranial growth during adolescence and a greater increase in the rate of facial growth.

From what has been stated previously in this paper it can be said as a useful generalization that the cranial type of growth depends upon expansion of the brain and orbital contents, while the facial type of growth derives its early impetus from the growth of cartilage, but is largely dependent, especially at the later stage, on surface deposition. Surface deposition is also responsible for the less marked increase in cranial dimensions which occurs in adolescence.

It is sometimes stated that growth in any dimension of the face or cranium is continuous and regular in nature. This belief is the result of using the mean values of large numbers of measurements within each age group. Analysis of the growth of individuals, however, shows that growth proceeds in an irregular and jerky manner, and that the pattern of growth varies to a considerable extent in each individual.

Table III gives the figures of total face height of six boys from Low's measurements (Low, 1952). Note the difference between the growth of individual cases and the type of growth suggested by the mean values for the series.

TABLE III

| Case No. | 3 days | 1 year | 2 years | 3 years | 4 years | 5 years | Total increase |
|---|---|---|---|---|---|---|---|
| 1 | 47 | 76 (29) | 80 (4) | 88 (8) | 88 (0) | 95 (7) | 48 |
| 2 | 55 | 67 (12) | 80 (13) | 92 (12) | 98 (6) | 102 (4) | 47 |
| 3 | 50 | 70 (20) | 78 (8) | 83 (5) | 92 (9) | 93 (1) | 43 |
| 4 | 51 | 68 (17) | 76 (8) | 87 (9) | 93 (6) | 100 (7) | 49 |
| 5 | 53 | 82 (29) | 82 (0) | 90 (8) | 90 (0) | 100 (10) | 47 |
| 6 | 57 | 82 (25) | 88 (6) | 92 (4) | 94 (2) | 94 (0) | 37 |
| Mean | 50·6 | 72·2 (21·6) | 78·7 (6·5) | 84·3 (5·6) | 88·5 (4·2) | 92·3 (3·8) | 42·7 |

The figures in brackets show the increase over the previous measurement.

There is also a change in the shape of both the cranium and face during childhood. The cranial index (breadth × 100/length) usually decreases slightly, while the facial index (height × 100/breadth) increases to a considerable extent; that is, the length of the cranium and the height of the face increase relative to their width. This is especially true in the case of the face.

More important information on head form and face form would be obtained if, in any given series, we could establish a means of estimating the degree of correlation between them. I have found it useful to classify the cranial and facial skeleton in each individual into one of the following classes: Long wide (Group A), Long narrow (Group B), Long moderate (Group C), Short wide (Group D), Short narrow (Group E), Short moderate (Group F), Moderate wide (Group G), Moderate narrow (Group H), Moderate (Group M), that is nine classes in all. The relationship between cranium and face can be expressed as being one of three degrees of harmony.

(1) Complete harmony, e.g. long wide cranium, with long wide face.
(2) Partial harmony, e.g. long wide cranium with short wide face.
(3) Disharmony, e.g. long wide cranium and short narrow face.

Table IV shows the distribution of cranial and facial types and the degree of harmony among 115 males from the town of Ballymoney in Northern Ireland.

TABLE IV.—GROUPS WITH % DISTRIBUTION

| | A | B | C | D | E | F | G | H | M |
|---|---|---|---|---|---|---|---|---|---|
| Cranium | 30 | 1 | 8 | 9 | 4 | 10 | 17 | 4 | 16 |
| Face | 29 | 6 | 7 | 15 | 4 | 6 | 15 | 4 | 14 |

Degree 1 harmony 26%
Degree 2 ,, 42%
Degree 3 ,, 32%

It will be noticed that although in both the cranium and face the long wide (Group A) type is the most common and that the number in each group is much the same for cranium and face, there is, in fact, no strict correlation between facial and cranial form.

In the facial skeleton itself various degrees of harmony or disharmony may exist between the form of its different parts such as the orbital cavities, nasal cavity and palatal region. It would seem that the forms of these various parts of the skull are under the control of independent genetic factors. Growth in facial height involves growth of the orbital cavities, nasal cavity and mouth region. Growth in facial width (bizygomatic) involves growth of the nasal cavity, orbital cavities and the flare of the zygomatic arches. Each of these regions has a different pattern of growth and the same total dimension in two individuals may have different contributions from each region.

Much work remains to be done on the growth of these individual parts of the facial skeleton and their correlation. Table V, which gives some measurements of two microcephalic skulls, illustrates the complexity of the problem.

TABLE V.—DIMENSIONS OF 2 MICROCEPHALIC SKULLS
(*Queen's University Anatomy Department*)

| | 1 | 2 | Range of 300 Scottish male skulls |
|---|---|---|---|
| Cranial capacity .. .. | 455 | 695 | 1,170–1,930 |
| Cranial length .. .. | 140 | 153 | 171–204 |
| Cranial width .. .. | 103 | 108 | 128–152 |
| Cranial base .. .. .. | 94 | 92 | 86–112 |
| Upper facial height .. .. | 68 | 62 | 57–83 |
| Orbital height .. .. | 32 | 34 | 28–39 |
| Bizygomatic width .. .. | 106 | 105 | 114–143 |
| Palatal width (internal) .. | 40 | 30 | 29–44 |

It will be seen that the cranial and bizygomatic measurements of both skulls are below the normal range, that upper facial height, orbital height and the cranial base length are within the normal range and that the palate width is close to the upper limit of the normal range in one skull and close to the lower limit in the other. The second skull, however, is edentulous.

Table VI gives the measurements of two acromegalic skulls (Geddes, 1911) and two hydrocephalic skulls (Queen's University, Anatomy Department).

TABLE VI.—DIMENSIONS OF TWO ACROMEGALIC AND TWO HYDROCEPHALIC SKULLS

| | Acromegalic | | Hydrocephalic | | Range of 300 Scottish male skulls |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | |
| Cranial capacity .. .. .. | — | — | 2,660 | 2,980 | 1,170–1,930 |
| Cranial length .. .. .. | 189 | 201 | 218 | 214 | 171–204 |
| Cranial width .. .. .. .. | 146 | 148 | 176 | 181 | 128–152 |
| Cranial base .. .. .. .. | 126 | 106 | 98 | 112 | 86–112 |
| Upper facial height .. .. .. | 98 | 82 | 69 | 76 | 57–83 |
| Orbital height .. .. .. | 40 | 36 | 31 | 37 | 28–39 |
| Bizygomatic width .. .. .. | 133 | 150 | — | 140 | 114–143 |
| Palatal width (external) .. .. | 63 | 70 | — | — | 49–70 |
| Palatal width (internal) .. .. | — | — | 38 | 43 | 29–44 |

*Note.*—No. 1 is a female.

In both the acromegalic skulls (Nos. 1 and 2) the cranial measurements are within the range of normal. In skull 1 the length of the cranial base, the upper facial height, and the orbital height are above the normal range. In skull 2, however, the cranial base length is within the normal range, bizygomatic width is above the normal, while the upper facial height and palate width are high up within the normal range. In the hydrocephalic skulls (Nos. 3 and 4) only cranial capacity, cranial length and cranial width are outside the normal range.

The measurements of these abnormal skulls show the independence of different regions of the skull and also the powers of compensatory growth. In the first microcephalic skull the failure of growth of the cranium has not affected growth of the palatal region. In the first acromegalic skull the great growth in facial height has not affected palatal width.

Recent work by Symons (1951) and Dixon (1953) on the mandible and maxilla indicates that these bones are built up of quite distinct developmental parts. These are the neural, alveolar, ramal and muscular processes in the mandible, and the neural, alveolar, zygomatic and palatal processes in the maxilla. The neural elements are related to the mandibular and infraorbital nerves, and the ramal element of the mandible corresponds to the zygomatic process of the maxilla in that both depend upon a mass of secondary cartilage for their growth. The muscular processes of the mandible are the angle and coronoid processes and are the only parts which depend on muscular function for their development. Moore and Hughes (1942), and Hughes (1942) concluded that multiple genetic factors were concerned with the development of the ramus, body, angle, alveoli and teeth in the mandible, and teeth, alveoli and body of the maxilla in the upper jaw. The independent origin of these parts increases the probability of such a gene-regulated developmental mechanism.

## DISCUSSION

The evidence brought forward in this paper, although incomplete, indicates that the growth of the human face after birth falls into two distinct phases:

(1) From birth to about the 7th year of age.

(2) After the 7th year.

During the first phase growth is, to a considerable extent, regulated by the cartilage of the nasal septum, cranial base and mandibular condyle. Growth takes place at the sutures as these are separated by the growth of the cartilage of the nasal septum and of the orbital contents. The orbital cavity is increasing in size and the Frankfort plane is not at this time a staple landmark. Growth is active in both the cranial and facial regions of the skull and at the junctional area between them (the cranial base). All parts of the cranial base are increasing in size. During this period the deciduous dentition is in use and the facial muscles are relatively more active and more fully developed than the muscles of mastication.

After the 7th year, that is during the second phase, growth of the nasal septum ceases and also growth at the facial sutures. Growth of the contents of the cranial and orbital cavities is almost complete as is the middle segment of the cranial base (pituitary fossa to foramen cæcum). The Frankfort plane becomes stabilized and with the completion of sutural growth the cranio-facial union becomes consolidated to meet the mechanical stresses associated with the use of the developing permanent dentition. In this phase growth of the facial skeleton is predominantly a matter of surface

deposition and internal reconstruction. The cartilages of the mandibular condyle and of the cranial base (spheno-occipital synchondrosis) continue, however, to function as important growth sites in thrusting the facial skeleton forwards from the vertebral column. The muscles of mastication reach their full development at the end of this period with the completion of the permanent dentition.

SUMMARY

(1) The cartilage of the cranial base, nasal capsule and Meckel's cartilage act as pace-makers for the early growth of the facial skeleton.

(2) The middle segment of the cranial base is complete by the 7th year and is the most stable region of the skull after that time.

(3) Growth at the facial sutures is secondary to a process of separation at the sutures which is produced by proliferation of cartilage and expansion of such organs as the brain and eyeballs.

(4) Growth of the face is intermittent in nature and differs in its pattern for different regions.

(5) The relationship in form between the facial and cranial regions of the skull may be harmonious or disharmonious.

(6) Analysis of skulls showing abnormal growth illustrates the developmental independence of various regions of the skull.

I wish to acknowledge my thanks to Professor J. J. Pritchard and Mr. N. B. B. Symons, M.Sc., B.D.S., for advice and criticism during the preparation of this paper, and to Mr. A. D. Dixon, M.D.S., for help in preparing the illustrations.

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## Comments on "The Solution of the Piltdown Problem"

By ALVAN T. MARSTON, F.D.S.

ON November 21, 1953, the British Museum (Natural History) published the *Bulletin*, Geology Vol. 2, No. 3. *The Times* of the same day published an article from "Our Museums Correspondent' on the "Piltdown Man Forgery—Jaw and Tooth of Modern Ape—Elaborate Hoax". On the same date the B.B.C. further publicized the matter in its news bulletins, and the Keeper of Geology of the British Museum (Natural History) also broadcast on the subject. There can be little doubt that it was a pre-planned and synchronized effort.

By 1952 I had succeeded in getting published fresh evidence relating to the Piltdown problem: "The relative ages of the Swanscombe and Piltdown skulls, with special reference to the Fluorine Estimation Test", in 1950*a*; "Reasons why the Piltdown canine tooth and mandible could not belong to Piltdown Man", which was submitted in 1950 but not published until 1952, although its salient features had been published in the Proceedings of the Geological Society of London for December 14, 1949 (Marston, 1950*b*), and finally my note on the "Human Mandibular Lacteon Constant" (*ibid*) had been published in *Man* (Marston, 1952*c*). The effect of these was to render the British Museum's attitude in presenting *Eoanthropus dawsoni* to the public as a "missing-link", untenable.

Nevertheless *Eoanthropus dawsoni* was allowed to figure in the Dome of Discovery, South Bank Exhibition in 1951, and in a somewhat similar exhibit in the Natural History Museum in 1952 and 1953, to explain the theory of human evolution from an ancestral ape, perhaps the Miocene *Proconsul*. This showed clearly a refusal on the part of the British Museum to face up to the facts of the evidence which I had published.

My 1952 paper (Marston, 1952*a*) contained sections to show that the worn Piltdown molars which had been claimed to be human, were as truly ape-like as true ape molars, and also that the wear on the canine tooth and on the molars was not human wear but was due to mandibular movement associated with the flat anthropoid type of temporo-mandibular joint, with long-crowned canine teeth which prevented outward lateral movement, and with rapid wear in a young ape in which although the canine and probably the third lower molar had erupted, yet also had incompleted roots.

In the British Museum 1953 Bulletin, on pages 141–2 it is alleged that the mandible and canine tooth are actually those of a modern ape (chimpanzee or orang) which have been deliberately faked to simulate fossil specimens. It is claimed that the results of their investigations have now demonstrated quite clearly that the mandible and canine tooth are indeed deliberate fakes. Because the authors are unable to understand the wear on the Piltdown teeth they ask us now to believe that someone took a modern ape mandible, broke it through near the symphysis, removed all of the teeth excepting $M_1$ and $M_2$, removed the bony septa, broke down the alveolus, scooped out the whole of the cancellous tissue below the whole extent of $M_1$, broke off the head of the condyle, carved up the sharp edges of the bone to make them round, reduced the backward extension of the simian shelf to make it less like a modern ape, filed down the occlusal surfaces of the molar teeth, scribed out, in order to make more definite, the margin of the talonid basin on $M_2$, made the occlusal surface of $M_1$ to be differently oriented from that of $M_2$, and the lingual border of $M_1$ to be out of direct alignment with that of $M_2$.

To confuse the issue further the supposed faker took an immature ape upper canine of the opposite side, filed down the biting surface in so surprising a manner as to make the contour of the lingual articular facet directly reciprocal to that of the antero-external surface of a first lower premolar as seen in orang; actually filled the open pulp-chamber with sub-angular grains of iron-stone and sand and plugged a larger stone into the open end to serve as a stopper to prevent the sand from falling out.

Was such arrant nonsense ever exceeded in scientific controversy?

I say that none of those teeth—neither canine nor molar—nor the mandible, has been filed or pared down as alleged; that the morphology of the crown and of the root, and the infilling of the pulp-chamber with sub-angular detritus from the gravel-bed showed that the canine was a fossil tooth and not from a modern ape, and because of the difficulty of matching it in modern apes it had been variously assigned to *Pan vetus*, *Troglodytes dawsoni*, or *Boreopithecus*.

In like manner the feeble development of the simian shelf indicates, as had never before been questioned, that the mandible was a truly fossil ape. Indeed Sir Arthur Smith-Woodward's own description of the finding of the jaw states that both he and Mr. Dawson—to quote—

> "We both saw half of the human lower jaw fly out in front of the pick-shaped end of the hammer which he was using" (The Earliest Englishman, p. 11, 1948).

## The Fluorine Content of the Teeth

F. J. Brekhus and W. D. Armstrong (1935) gave the fluorine content of sound human dentine as 0·0169%, and from teeth affected by fluorosis as from 0·0371 to 0·0504%.

The Museum Bulletin claims that the left lower Piltdown ii molar found two miles away on a heap of stones raked from the surface of a field, now belongs to the Piltdown mandible. Its fluorine content is given as $< 0{\cdot}01\%$; those of the Piltdown mandible $< 0{\cdot}04\%$ although the same blood stream supplied both sides of the jaw; and they compare these with the value for a molar of Recent chimpanzee $< 0{\cdot}06\%$ with six times the amount contained in the now supposed ape Piltdown ii molar!

The absurdity of claiming that the molars of the right side of the jaw contained four times the amount of fluorine in that of the left side, is obvious from my findings that the molars of the right side, when measured at the neck, were narrow and the teeth were worn in an anthropoid manner, whereas the molar from Piltdown ii was wide at the neck and was worn in a human manner. The Piltdown ii molar could not belong to the Piltdown mandible.

## The Evidence of the Organic Content

It was recounted at the Geological Society (25.11.53) how, when drilling into the mandible, a smell of "burning" was noticed. This mandible is now claimed to be a modern "fake". I have seen the mandible and where the bone has been drilled, and have drilled into a modern mandible in the same situation without producing any smell of burning, and have also drilled into bones of 300,000, 100,000, 30,000 years, Holocene age, and one from the previous Sunday's joint, using a No. 10 rose-head, without producing the smell of burning. Some other reason than that of modernity should be sought to explain the smell of burning, e.g. the non-malevolent use of a preservative.

## The Chromate Staining

The knowledge that some of the bones had been treated with potassium bichromate did not prevent Dr. A. T. Hopwood (1934) from concluding—

> "The Piltdown remains represent a type of humanity which lived in this country at the beginning of the Pleistocene, and which had for contemporaries a very primitive elephant, the last of the European Mastodonts, and a hippopotamus."

My own suggestion is that Mr. Dawson might first have soaked the bones which he found before the "official dig" in gelatine solution (size) to harden them, and later might have used potassium bichromate to render the gelatine insoluble; unfortunately it altered the colour.

> "When mixed with potassium bichromate, and exposed to light, gelatine becomes insoluble in water." (Cohen, J. B., Theoretical Organic Chemistry, London, 1908.)

In view of the semi-concreted nature of the lenticle of gravel from which Smith Woodward saw the mandible "fly out"—and anyone who has had actual field experience in working a semi-concreted deposit will recognize the ring of truth in the expression "fly out"—it would appear that the chromate treatment of the mandible occurred later, and after Smith Woodward had seen its original condition.

## Conclusion

I have examined with a lens of 20 × magnification every millimetre of the Piltdown mandible and its two molar teeth, the Piltdown canine and the Piltdown ii left lower molar, and state that, apart from the drilled cavities made for taking test-samples, neither the teeth nor the mandible have been mutilated in any way.

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The following is a copy of a "Notice of Operation" sent out by Mr. Marston as long ago as November, 1936.

## NOTICE OF OPERATION

*Eoanthropus dawsoni* is about to undergo a major dental operation on Monday, November 23, at the next meeting of the Odontological Section of the Royal Society of Medicine, at 8.0 p.m.

The operation will involve the extraction of the right lower canine tooth and the excision of the mandible. The condition of this tooth and of the mandible which has long been a serious problem, has at length been accurately diagnosed.

After excision, it is proposed to offer the removed parts to the British Museum (Natural History) to be placed in the section of fossil anthropoids.

*Eoanthropus* has been so heavily doped that no anæsthetic will be considered necessary. Assistance may be needed, however, in holding the victim down.

*Eoanthropus* is expected to make a speedy return to convalescence. The prognosis is good. His mental outlook will be more human. He will be less anti-social without a mandible which has prevented him from eating and speaking like a human being.

*Dental Surgeon.*—A. T. Marston, L.D.S.

*Assistants.*—You.

Copies of this to be posted up on the Notice Boards were sent to the British Museum (Natural History), The Royal College of Surgeons, and to the different London Dental Schools.—A. T. M.

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# Section of the History of Medicine

President—The Right Hon. Lord WEBB-JOHNSON,
K.C.V.O., C.B.E., D.S.O., T.D., M.B., F.R.C.S., LL.D.

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## Medical Aspects of the Assassination of Abraham Lincoln

By HUGH R. GILMORE, Jr., Colonel, M.C., U.S.A.
*Curator, Medical Museum, Armed Forces Institute of Pathology, Washington* 25, *D.C.*

THE medical aspects of the story of the assassination of Abraham Lincoln are more varied than might be expected. The location of the death wound on the left side of the head rather than on the right is puzzling. Even though an autopsy was performed, disagreement exists as to the course of the bullet. Injuries to the skull opposite the wound of entrance have aroused speculation as to their mechanism. Booth's injury incurred in his dramatic leap to the stage and his visit to Dr. Mudd involved this doctor as a possible conspirator. The shooting of Booth at his capture and his subsequent death resulted in another autopsy and involved the identification of the body from a surgical scar.

The assassination took place at Ford's Theatre in Washington, D.C., on the night of April 14, 1865. This was Good Friday, and on the previous Palm Sunday, Lee had surrendered to General Grant. Washington was in a jubilant mood, for the war was over and the victorious North was celebrating. Mrs. Lincoln thought a theatre party appropriate, and Lincoln, who enjoyed the theatre, fell in with her plan and asked General and Mrs. Grant to accompany them. General Grant accepted, and the newspapers announced that the Lincolns and the Grants would attend Ford's Theatre on the night of the 14th. Subsequently the Grants declined because they were leaving the city. Another couple, Major Henry Reed Rathbone and his fiancée, Miss Clara Harris, daughter of Senator Harris of New York, completed the party. About 9 o'clock on a rather unpleasant, foggy, raw spring night, the presidential party arrived at the theatre and occupied a previously prepared box which was at a height of 12 feet above the right side of the stage.

This box had been made ready not only by the theatre management but also, unknown to the management, by the assassin, John Wilkes Booth, who as an actor had easy access to the theatre. Booth had bored a hole in the door leading to the box to provide a peephole through which he could observe its occupants and the events on the stage. He had also prepared a wooden bar which could be used to prevent entrance through the door leading from the theatre to the vestibule of the box.

Booth's heredity is of interest in view of his actions. His great grandfather had been a silversmith in Bloomsbury, London, and his grandfather, Richard Booth, was a lawyer who was known as an anti-royalist and an ardent republican. At one time, Richard Booth had attempted to secure a commission in the American revolutionary forces. Richard Booth's eldest son was named Junius Brutus, indicating his father's admiration for the slayer of imperial Julius Cæsar. Junius Brutus Booth, who was to become the father of John Wilkes, came to America from England in 1821 and became one of the outstanding actors of his day. His close associates knew him as an eccentric and a man of unsteady temperament. His heavy drinking sometimes interfered with his acting, and to keep him sober for his performances, his managers held a close watch on him. It is told that once, when he had been locked in his theatre dressing room to keep him from drinking, he bribed a boy to bring a bottle to the door and, with a straw through the keyhole, satisfied his thirst [1]. On one occasion, he was narrowly prevented from stabbing an acquaintance merely because he felt he had to cut someone's throat [1]. John Wilkes Booth, his ninth child, was named for a noted London advocate of people's rights, who became Lord Mayor of London in spite of the enmity of George III and who was a hero to the Booth clan.

With this family background, it is not surprising that John Wilkes Booth followed his tragic course. He was 27 years old in 1865 and had established himself as a fair actor, although not the equal of his brother Edwin. He was born on a Maryland farm near Baltimore and along with many other Maryland citizens, was a Southern sympathizer. His sympathies, however, did not extend to donning a Confederate uniform. He chose instead to remain an actor and a plotter. In 1864, he organized a group which had as its objective the kidnapping of President Lincoln; one attempt was actually made, but fortunately the plot miscarried.

Booth was a handsome man, a good marksman, and a skilful fencer. He inherited the unstable Booth temperament and the family antipathy for recognized authority. "Sad, mad, bad John Wilkes Booth" was the description given by the actor Sir Charles Wyndham [1].

The plot directed by Booth on this April night included three accomplices. A physically powerful 20-year-old veteran and deserter from the Confederate Army, Lewis Paine, was originally given the

task of killing Grant when it was announced that Grant was to accompany Lincoln to the theatre. When it was learned that Grant had left Washington, Paine was assigned to kill the Secretary of State, William H. Seward, and Paine very nearly accomplished his mission. On the night of the 14th, he entered the Seward house on Lafayette Square on the pretext of delivering medicine for the Secretary who was in bed suffering from a fractured jaw. A servant attempted to stop him at the door, but he hurried up the stairs where Seward's son Fred grappled with him; Paine struck young Seward on the head with his pistol and knocked him unconscious, fracturing his skull. Seward's daughter and a soldier nurse, Sgt. George T. Robinson, were in the bedroom with the Secretary, but both were thrust aside and Robinson was cut by Paine's knife. Paine stabbed at Seward and cut him about the face and neck, but Seward's life was saved by the iron brace which was used to support the fractured jaw. Seward rolled from the bed between the bed and the wall, and Paine then made his escape after wounding another son, Augustus, who had hurried to the room on hearing the disturbance [2].

A second conspirator was George A. Atzerodt, a carriage maker from Port Tobacco, Maryland. His assignment was to kill Vice-President Andrew Johnson, but Atzerodt lost courage and failed to make any attempt on Johnson's life. David E. Herold, a 20-year-old drug store clerk, was to guide Paine to the Seward house and out of Washington. He fled when he heard shouts for police coming from the Seward house and joined Booth in his flight.

Seward's life was saved by a fractured jaw and Vice-President Johnson was spared by loss of heart on the part of the assigned assassin, but the life of Lincoln was not spared. John Wilkes Booth was only too successful in the execution of his part of the plot.

The box occupied by the President and his party could be divided into two boxes by a removable partition, and doors from each of the boxes opened to a vestibule leading to the balcony (dress circle). On this occasion, the partition was removed, and a rocking chair with a high back was placed in the box near the wall which separated the box from the balcony. This chair blocked the inward swinging door leading to this half of the box, and this chair was occupied by the President, placing him directly in line with the door in which Booth had previously bored the peephole [3]. Mrs. Lincoln sat beside her husband on his right, and Miss Harris and Major Rathbone occupied the half of the box nearest the stage. The party entered the box through the one available door [4] which was at the end of the vestibule leading from the balcony to the box, and this same door was supposedly used by Booth, who thus approached from the President's right. Booth chose a time in the third act when only one actor was on the stage. This was between 10 and 10.30. Watching through the peephole, he seized the opportune moment and, slipping quietly into the box, shot Lincoln in the back of the head with a Derringer pistol, a weapon about 6 in. long, firing a ball ½ in. in diameter. The bullet entered about an inch to the left of the mid-line and at a level which tore the left lateral (transverse) sinus.

With Booth approaching from Lincoln's right, why was the wound on the left side of the head? One witness, James P. Ferguson, a restaurant keeper, testified at the conspiracy trial: "The President, at the time he was shot, was sitting in this position: he was leaning his hand on the rail, and was looking down at a person in the orchestra—not looking on the stage. He had the flag that decorated the box pulled around, and was looking between the post and the flag" [7]. In this position, the left side of Lincoln's head would have been presented to Booth as he approached from the President's right, and a wound on the left side is explained. Without this movement by Lincoln, the assassin could not have shot him on the left side without first passing behind Mrs. Lincoln and the President himself.

Although an autopsy was performed, the course of the bullet is in doubt. The autopsy was done by an army doctor who was on duty at the Army Medical Museum, Assistant Surgeon J. J. Woodward, assisted by another army doctor, Assistant Surgeon Edward Curtis. Woodward's handwritten report of the autopsy is very brief but concise. According to his observation, the bullet "... entered through the occipital bone about an inch to the left of the median line and just above the left lateral sinus which it opened. It then penetrated the dura mater, passed through the left posterior lobe of the cerebrum, entered the left lateral ventricle and lodged in the white matter of the cerebrum just above the anterior portion of the left corpus striatum where it was found.... The ventricles of the brain were full of clotted blood. A thick clot beneath the dura mater coated the right cerebral lobe. There was a smaller clot under the dura mater of the left side. But little blood was found at the base of the brain. Both the orbital plates of the frontal bone were fractured, and the fragments pushed up toward the brain. The dura mater over these fractures was uninjured. The orbits were gorged with blood."[1]

This report clearly indicates that the bullet lodged in the left side of the brain. However, at least two other doctors who witnessed the autopsy reported the bullet as crossing the mid-line and lodging in the right cerebrum. Dr. Charles S. Taft was one of the first doctors to reach Lincoln in the theatre and remained at the bedside until his death. He was also present at the autopsy and wrote an account of Lincoln's death in which he stated that the bullet crossed the mid-line and lodged in the "... anterior

[1]From photostat copy on file at the Medical Museum of the Armed Forces Institute of Pathology, Washington, D.C.

lobe of the cerebrum immediately behind the right orbit" [8]. Surgeon-General Barnes was also at the autopsy and two years later he testified at the Surratt trial that, "The ball entered the skull to the left of the middle line and below the line with the ear. It ranged forward and upward toward the right eye, lodging within half an inch of that organ" [9]. Another witness at the autopsy, Dr. Robert King Stone, Lincoln's personal physician, testified in 1865 at the trial of the conspirators that ". . . the ball was found in the anterior part of the same side of the brain [as it had entered], the left side. . . ." [5].

Further inconsistencies appear in observations on pupillary changes. Dr. Charles A. Leale [10], who also attended Lincoln, noted, ". . . the pupil of that eye (left) was slightly dilated, the right pupil was contracted; both were irresponsive to light." This conflicts with the statement by Dr. Taft [8] that ". . . the left pupil was much contracted and the right widely dilated; total insensibility to light in both." Both observations were made after the President had been moved from the theatre. Such disagreement among competent witnesses cannot be reconciled by historians of to-day.

Another controversial point is the explanation of the comminuted fractures of the two orbital plates. All evidence indicates that the bullet stopped short of the frontal portion of the skull, so the fractures of the orbital plates must have been due to an indirect force.

The case was referred to in the "Medical and Surgical History of the War of the Rebellion" [10] as an example of possible fracture by contre-coup, but the author of this volume, Assistant Surgeon George A. Otis, was inclined to reject this theory in favour of a theory proposed by Professor T. Longmore of Netley, England, Professor of Military Surgery at the British Army Medical School [12]. "This double fracture was decided to have been caused by contre-coup. If the term contre-coup be limited to its precise significance of 'counter-stroke'—i.e. the impression made by the stroke on the part of the cranium opposite to that directly struck by the ball—will the force of contre-coup explain the fracture in this instance; It seems very difficult to conceive that the orbital plates could be fractured by such a counter-stroke, while the portion of the cranial arch opposite to that which received the primary blow, including the expanse of the frontal bone and the several processes within which the orbital plates are held, and, by which they are so strongly protected in all directions laterally, remained entire and unchanged. I am inclined rather to attribute the lesions mentioned to a transmitted undulatory stroke or sudden impulse of the brain substance itself against the thin bony layers constituting the orbital plates."

Dr. J. A. Ashhurst, Jr. [13] of Philadelphia, in his review of the first volume of the "Medical and Surgical History of the War of the Rebellion", made the following comments on these fractures and on the explanations suggested by Doctors Otis and Longmore:

"The most remarkable pathological feature of President Lincoln's case was the fact that both orbital plates of the frontal bone were fractured, the fragments being pushed upwards towards the brain, while the ball, which had entered through the occipital bone, was found lodged in the brain above but not in contact with the broken orbital plates. The latter were regarded [by doctors at the autopsy] as having been fractured by contre-coup, but Dr. Otis, adopting the suggestion of Professor Longmore, considers it a more plausible explanation, that the force of the ball's impulse was transmitted directly through the cerebral mass itself, and accounts for the peculiar displacement of the orbital plates by supposing that they were pushed upwards by the pressure of the blood extravasated within the orbits. With due diffidence we must confess that we are not satisfied as to the correctness of this theory, and venture to express the opinion that the true explanation of the lesion in question is somewhat different. With regard to the subject of contre-coup, it has always seemed to us that a great deal of unnecessary confusion is created by the want of agreement among surgical writers, as to precisely what is to be understood by the term; if the word is to be used in its most limited sense, as applying solely to an isolated fracture, caused by violence applied to a part diametrically opposite to the point of injury, probably the orbital fracture in President Lincoln's case may not, as Professor Longmore remarks, be regarded as a fracture by counter-stroke; but, on the other hand, if the word is to be used in a broader sense, as applying to an isolated fracture caused by transmitted or indirect violence, the lesion being at a distance from the point at which the injury is received, then President Lincoln's case affords as fair an example by contre-coup as can be asked for.

"The true explanation of this case is, we believe, to be found in a study of the considerations advanced by Saucerote, Sabouraut, Chopart, and Delpech [14], in their writing on the subject of contre-coup, which considerations, though not in fashion with modern pathologists, have always seemed to us eminently reasonable. The theory which was propounded by the writers referred to, is, as is well known, that the skull (like any other spherical or ellipsoidal hollow body) undergoes, when struck, certain changes in shape, the diameter corresponding to the point of impact being first shortened while the transverse diameter is lengthened, and being subsequently lengthened while the transverse diameter is shortened, these alternate oscillations in form continuing until the force of the blow has been exhausted, when the parts return to a state of rest. Now, the first effect of a ball striking the occipital bone (as in President Lincoln's case) would be, according to this theory, to shorten the antero-posterior diameter of the skull, and lengthen the lateral diameters drawing all parts in front (including the orbital plates) inwards toward the brain, and pressing the lateral portions outward. But bearing in mind that in cases of fracture by transmitted violence the weakest parts

always give way—the orbital plates in this instance were, according to Dr. Otis, 'unusually thin'—and bearing in mind Teevan's rule, that fracture invariably begins in the line of extension, what should we expect but that the weakest parts (the unusually thin orbital plates) should yield, and that they should yield in the line of extension, viz., inwards toward the brain; and this is precisely what was found in President Lincoln's case after death. This explanation (which is merely an application of the old doctrine of contre-coup), seems to us, upon the whole, more satisfactory than Dr. Otis's theory of displacement by the pressure of blood extravasated within the orbits. As to the fracturing impulse being transmitted through the cerebral pulp, we confess that it seems to us much more probable that the force should pass around through the walls of the skull itself; the brain mass, measurably approximating in structure to a fluid, would, we should suppose, tend to diffuse force equally in all directions, rather than to transmit it with such concentration as to lead to the occurrence of fracture."

The reader is offered these several explanations and may take his choice or frame his own theory. To the writer, the explanation given by Dr. Ashhurst seems most reasonable.

A few words might be said about the medical care given President Lincoln after the shooting. Three army doctors in the audience rushed to the box—Dr. Charles A. Leale, Dr. Charles S. Taft, and later Dr. Albert F. A. King. The wound was located and artificial respiration applied, for the patient was pulseless and his breathing was hardly evident. He responded somewhat and about fifteen minutes after the shooting he was carried to a house across the street, since it was thought he could not survive the ride of a mile or so to the White House. He was given a little brandy which he swallowed, but later attempts to give brandy were unsuccessful. Sinapisms were applied together with blankets and hot water bottles. The following notes are from Dr. Taft's account [8]. "The left upper eyelid was swollen and dark from effused blood; this was observed a few minutes after his removal from the theatre. About thirty minutes after he was placed upon the bed, discoloration from effusion began in the internal canthus of the right eye, which became rapidly discolored and swollen with great protrusion of the eye. . . . The only surgical aid that could be rendered consisted in maintaining the head in such a position as to facilitate the discharge of the wound, and in keeping the orifice free from coagulum. . . . While the wound was discharging freely, the respiration was easy; but the moment the discharge was arrested from any cause, it became at once labored. It was also remarkable to observe the great difference in the character of the pulse whenever the orifice of the wound was free from coagulum and discharged freely; thus relieving, in a measure, the compression. This fact will account for the fluctuations in the pulse as given in the subjoined notes.

"About 2.00 a.m. an ordinary silver probe was introduced into the wound by the Surgeon-General. [Surgeon-General Barnes together with Lincoln's family physician, Dr. Robert King Stone, had assumed charge of the patient.] It met an obstruction about three inches from the external orifice which was decided to be the plug of bone driven in from the skull and lodged in the track of the ball. The probe passed by this obstruction, but was too short to follow the track the whole length. A long Nélaton probe was then procured and passed into the track of the wound for a distance of two inches beyond the plug of bone, when the ball was distinctly felt; passing beyond this, the fragments of the orbital plate of the *left* orbit were felt. The ball made no mark on the porcelain tip and was afterwards found to be of exceedingly hard lead." (Surgeon-General Barnes testified [9] that the bullet was made of brittania metal—a mixture of antimony, tin, and copper.)

"Some difference of opinion existed as to the exact position of the ball, but the autopsy confirmed the correctness of the diagnosis upon first exploration." (Yet Taft's account of the autopsy places the ball on the right side.)

Dr. Taft listed observations on the pulse and respirations, ". . . noted down by Dr. A. F. King at the bedside . . .

10.55—48.
11.24—42, respirations, 27 per minute, breathing quiet.
11.47—45, respirations 24, stertorous.
12.10—48, irregularly intermittent.
12.28—60.
12.49—84, respirations 28.
1.00—100.
1.15—92.
2.10—60, respirations 34.
2.37—48.
2.54—48, much weaker, more thready; respirations feeble.
4.18—60, respirations 27, strong and stertorous.
5.40—64, thready, respirations 27.
6.25—thready, not counted; respirations 22; inspirations jerking.
6.45—respiration uneasy, choking and grunting; lower jaw relaxed; mouth open; a minute without a breath; face getting dark.
7.00—still breathing at long pauses.
7.20—died."

As Lincoln lay dying, what of the assassin? After the fatal shot was fired, Booth fought off the restraining hands of Major Rathbone with a slash of his knife and shouted, "Sic semper tyrannis", and then hobbled across the stage and out the stage door where a horse awaited him. In his dramatic leap from the box, Booth's spur caught in a flag used to decorate the box and caused him to land on the stage in such a manner that he broke the lower end of the fibula of his left leg.[1] In spite of this injury, he reached his horse safely and fled before anyone could stop him. He crossed over the Anacostia River out of Washington and into Southern Maryland, accompanied by only one accomplice, Herold, who caught up with Booth *en route* to Surrattsville (now Clinton, Maryland). The plotters had deposited carbines, blankets and whiskey at a tavern operated by John Lloyd in Mrs. Surratt's house and after obtaining these supplies, they proceeded to the house of Dr. Samuel A. Mudd near Bryantown, Maryland. They arrived about 4.00 a.m. of the 15th and Dr. Mudd attended to the broken leg and put Booth to bed. This care rendered to the assassin caused Dr. Mudd to be accused as an accomplice, and he was tried and convicted and sentenced to prison, but he was pardoned in 1869 by President Johnson.

Booth and Herold left Dr. Mudd's house hurriedly about 4.00 p.m. on the 15th when they learned that Federal troops were at Bryantown. For several days, they hid in the woods near the farm of Samuel Cox awaiting an opportunity to cross the Potomac River into Virginia. On Sunday morning, April 23, they landed on the Virginia shore and, about eight o'clock that night, reached the home of Dr. Richard Stewart who had been recommended to them.

But Dr. Stewart did not welcome the fugitives to his home. He gave them food and directed them to a cabin of a freed Negro, William Lucas, where they spent the night of the 23rd.

Booth was much disturbed by Dr. Stewart's lack of hospitality and sent this note to the doctor [15]:

"Dear Sir: Forgive me, but I have some little pride. I hate to blame you for your want of hospitality; you know your own affairs. I was sick and tired with a broken leg, in need of medical advice. I would not have turned a dog from my door in such a condition. However you were kind enough to give me something to eat, for which I not only thank you, but on account of the reluctant manner in which it was bestowed, I feel bound to pay for it. It is not the substance, but the manner in which a kindness is extended, that makes one happy in the acceptance thereof. The sauce in meat is ceremony; meeting were bare without it (Macbeth III, 4). Be kind enough to accept the enclosed two dollars and a half (though hard to spare) for what we have received.

Yours respectfully,
Stranger"

On the 24th, Lucas took Booth and Herold to a ferry which crossed the Rappahannock River to Port Royal, Virginia. On the ferry they met three Confederate soldiers and Booth made known his identity as the slayer of Lincoln. The soldiers helped the fugitives to the farm of Richard H. Garrett between Port Royal and Bowling Green and here they found shelter.

Booth's capture did not come until April 26, when he and Herold were trapped by a group of soldiers in a tobacco barn on the Garrett farm about 70 miles south of Washington. Herold surrendered but Booth refused, and to force him from the barn, it was fired. Booth was shot as he approached the door, by Sgt. Boston Corbett. Some doubt exists as to whether or not Booth may have shot himself, but Corbett insisted that he had fired the shot [6]. He was arrested and held for court-martial but was released by Secretary of War Stanton.

Booth lived about two hours after he was shot, dying about 5.30 a.m. on April 26 on the porch of the Garrett farm house. Herold, together with Atzerodt and Paine, was later tried and executed by hanging.

Booth's body was brought up the Potomac River to Washington on the Union Gunboat *John S. Ide* and transferred to the monitor *Montauk* at the Washington Navy Yard, where an autopsy was performed under the direction of Surgeon-General Barnes. Among witnesses who identified the body was Dr. John F. May of Washington. He had removed a "fibroid" tumour from Booth's neck over a year previously and was called to identify the body by the scar. Dr. May [16] stated that when he operated on Booth, he warned him that he must remain quiet till the wound healed, but Booth disregarded the warning and returned to his acting before the wound was properly healed. In a love scene with actress Charlotte Cushman, the lady, in placing her arms about his neck, inadvertently tore the wound open and as a result, the scar appeared more like a burn than a knife wound. Dr. May gave a perfect description of the wound before examining the body and thus the identification was satisfied.

The "Medical and Surgical History of the War of the Rebellion" [11] contains a description of the course of the bullet from the report of the autopsy performed on Booth. The damaged vertebra and spinal cord removed at the autopsy are deposited in the Medical Museum of the Armed Forces Institute of Pathology in Washington.

The story of Lincoln's death includes many controversial points which cannot be resolved.

[1] Accounts vary as to which bone was broken. Correspondence on file at the Medical Museum of the Armed Forces Institute of Pathology, Washington, D.C., includes a statement by Assistant Surgeon J. J. Woodward that it was the left fibula.

Booth's manner of entrance to the box is not commented upon by most historians. No one saw him enter the box and so it is not known which door he used. Neither door was locked and he may have been able to open the door behind Lincoln's chair sufficiently to slip into the box, in which case a wound on the left side of the head would be no mystery. If Ferguson is correct in saying that Lincoln was shot while leaning forward to look down toward the back of the theatre, the bullet entering the left side of the head would have been directed toward the right frontal area thus bearing out the statements of Dr. Taft and Surgeon-General Barnes and refuting the autopsy record and Dr. Stone's testimony.

The problem of the fractured orbital plates is the problem of skull fractures arising at a point distant to the point of impact, or as Hippocrates expressed it, "The bone is broken in another part of the head than that in which the man received the injury" [17]. The mechanism of these fractures still affords discussion in modern medical journals, and writers are not agreed as to the various theories which have been advanced.

It is doubtful if modern medical practice could have saved Lincoln's life, and the doctors in charge of the patient probably did all that could have been done. The probing of the wound with a non-sterile probe (Dr. Taft speaks of using a finger [8]) was of no help and would no doubt have led to infection if Lincoln had lived longer.

Booth's dramatic leap to the stage with the resultant fracture of his leg was a handicap to his flight and was a factor in his capture.

There is no doubt that Dr. Mudd was acquainted with Booth, but it is not known whether he knew that Booth had shot Lincoln when Booth presented himself for treatment. Certainly Dr. Mudd must have suspected that his patient was the assassin when he learned that Lincoln had been shot.

Dr. Mudd was imprisoned at Fort Jefferson on Dry Tortugas, one of the Florida Keys. He is said to have been of help in a yellow fever epidemic which spread through the area [18], and this circumstance may have influenced President Johnson to grant a pardon.

Booth had no regrets for his act but was disappointed that he was not hailed as a hero. He made the following entries in his diary on April 21 while hidden in the swamps of Southern Maryland.

". . . I am here in despair and why? For doing what Brutus was honoured for—what made Tell a hero. And yet I, for striking down a greater tyrant than they ever knew, am looked upon as a common cut-throat. . . . I struck for my country and that alone. . . . I do not repent the blow I struck. I may before God but not to man. I think I have done well. Though I am abandoned with the curse of Cain upon me, when, if the world knew my heart, that one blow would have made me great, though I did desire no greatness."

Booth pictured himself as the avenger of the South but his bullet silenced the most magnanimous, the most forgiving spirit of our times—the one man who might have helped the South. The man who had uttered these words at his second inauguration only a few weeks before his death:

"With malice toward none; with charity for all; with firmness in the right, as God gives us to see the right, let us strive on to finish the work we are in; to bind up the nation's wounds; to care for him who shall have borne the battle, and for his widow, and his orphan—to do all which may achieve and cherish a just and lasting peace among ourselves, and with all nations."

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# Section of Surgery

President—Sir HENEAGE OGILVIE, K.B.E., D.M., M.Ch., F.R.C.S.

[*November* 4, 1953]

## DISCUSSION ON CARCINOMA OF THE CARDIAC END OF THE STOMACH

**Professor J. F. Nuboer** (*Utrecht*): All those who have practical experience of the surgery of œsophageal carcinoma are acquainted with the melancholy fact that late results are exceedingly disappointing. Almost all patients who stood the operation successfully at first, prove to have succumbed to metastasis after some three years.

A favourable exception is that of carcinoma of the distal end of the œsophagus, and the cardiac portion of the stomach. In these cases prognosis is much more favourable. Sweet (1952) calculated that 17·5% of his cases were still alive after a period of five years; this figure rose to 40% when it related only to patients who were free from metastasis of the lymphatic glands.

The results obtained in the Surgical Department of the State University of Utrecht are broadly the same.

Surgical treatment of cardial carcinoma has always been a subject of special interest in Holland. In 1913 Zaaijer (of Leyden) was the first to remove a cardial cancerous tumour successfully. In 1942 I was the first in Holland to bring to a successful conclusion a case of cardial carcinoma, by means of resection of the œsophagus and the stomach, with subsequent intrathoracic œsophago-gastrostomy (Nuboer, 1944). This technique differed from that advocated by Adams and Phemister (1938) and it has since been followed by us.

Up to July 1, 1953, our Department had numbered 149 patients suffering from a malignant tumour at the junction of œsophagus and stomach. Although the diagnosis of this condition has greatly improved of late years, yet it is a fact that the greater number of these patients come too late for surgical treatment. In only 90 (out of the above-mentioned 149) cases did it prove possible to remove the tumour; in 35 cases resection was only palliative since metastasis had occurred in the liver and elsewhere, so that surgical therapy with curative intent was only possible in 55, or 37% of the total number. It must be deeply regretted that the greater part of these patients arrived too late for treatment, for when an operation for cardial carcinoma is performed in good time the prospects of recovery are comparatively favourable.

In nearly all cases stenotic symptoms are prominent, and they call for surgical treatment in the first place. If, therefore, the tumour cannot be removed *in toto*, it is desirable to perform a gastro-œsophageal resection with palliative intent. Although the risk of this operation on palliative grounds is somewhat greater than when it is performed for curative reasons, yet I believe that there are good reasons for it, since it is by no means rare for the patient to remain in comparatively good condition for about two years before metastasis causes him to succumb. Local recurrence was observed by us on only two occasions. In both cases the tumour had extended farther in the œsophageal submucosa than was supposed. When the tumour cannot be removed we must proceed to other palliative measures, which we shall mention presently.

Histological examination revealed that in the majority of our patients there was found adenocarcinoma. In 90 cases of œsophago-cardial resection there were 59 cases of adenocarcinoma, 8 of carcinoma solidum, 3 of carcinoma simplex, 3 of carcinoma papillare, 9 of epidermoid carcinoma and on 8 occasions we observed an undifferentiated carcinoma. The distribution of these figures contrasts strangely with results in England and America. Sweet (1952) observed 93 cases of adenocarcinoma, as against 99 of epidermoid carcinoma. Although adenocarcinoma extends probably earlier in the lymphatic glands than epidermoid carcinoma, Sweet's figures show that the prognosis of the two types of tumours is the same.

In view of the appropriate surgical therapy it is important to trace how carcinoma of the gastro-œsophageal junction (which we shall briefly call cardial carcinoma) usually spreads. We must premise that in by far the most cases it is impossible to establish whether the tumour originated primarily in the stomach or in the œsophagus. It is certain that the borderline between the two organs does not constitute a barrier to the growth of the tumour, and that in some cases it extends more in the direction of the œsophagus, in other cases more in the direction of the stomach. Its extension in the wall takes place chiefly in the submucosal layer, and it may extend considerably beyond the visible and palpable rim of the tumour. Although we can always establish that the tumour grows in the œsophageal wall in an oral direction, yet we get the impression that in most cases its extension over larger areas takes place in a distal direction; consequently the tumours at the junction of stomach and œsophagus are almost all observed on the gastric side of this borderline.

We may further establish that its growth along the lesser curvature in nearly all cases takes place over greater distances than on the greater curvature. We shall suggest an explanation when we discuss metastasis in lymphatic glands. In a number of cases the tumour pierces the wall of œsophagus and stomach, thus spreading in the contiguous tissues. It may infiltrate the mediastinal pleura, pericardium,

diaphragm, spleen, left lobe of the liver, pancreatic tail and left suprarenal gland. Such an extension need not prevent successful extirpation of the tumour and permanent recovery of the patient, although in most cases the operation in such circumstances must be looked upon as a palliative measure. The anatomical conditions in the vicinity of the distal part of œsophagus and cardia render it possible to make a more radical, local, and regional resection of the tumour than would be the case in the tumours higher in the œsophagus. When it has perforated the gastric wall, and has led to peritoneal metastasis, we must look upon the tumour as incurable.

Its extension along the lymphatic channels mostly takes place in accordance with a certain plan, and it differs somewhat from what we should expect after having studied the lymphatic channels and glands of this region. The paracardial glands and the glands along the left gastric artery are involved at a very early stage.

In all our cases we found that some (occasionally many) glands of this group were affected. The glands round the cardia in the mediastinum are frequently involved in the process. This is less often the case with the glands situated in the hilum of the spleen, which obtain lymph from the gastric fundus. At a later stage we may note infiltration of the glands along the cœliac artery, those along the aorta, together with those along the upper rim of the pancreas.

The lymph of the lesser curvature is chiefly drained in an oral direction, towards the glands round the cardia and along the left gastric artery. As mentioned before, we shall observe in the vast majority of the cases that these glands are infiltrated at an early stage, so that they are blocked up for the lymph stream. Hence the lymph from the region of the lesser curvature (like that from the region of the cardia) will have to seek other outlets. In such circumstances the lymph stream is usually reversed, so that in our case it moves towards the glands nearer to the pylorus on the lesser curvature.

This reversal of the lymph stream may cause the tumours in the region of the cardia to spread distally, particularly along the lesser curvature.

When all these possibilities of extension of a tumour are considered, we need hardly explain that in operable cases one has to proceed to a comprehensive operation. A tumour penetrating into the wall of œsophagus and stomach, or even perforating it, does not present insuperable problems. Resection will have to take place, orally and distally, at least two (preferably three) fingerbreadths beyond the visible and palpable rim of the tumour. In the region of the distal part of œsophagus and cardia the anatomical conditions are also favourable with regard to a wide extirpation. If necessary, the mediastinal pleura on one or both sides of the tumour must be sacrificed; part of the pericardium, of the lung, and of the diaphragm must follow; or the left lobe of the liver, the pancreatic tail, and the left suprarenal gland must be partly or entirely resected. I am of opinion that it is advisable to remove the spleen in all cases, for it is by no means rare for the lymphatic glands at the hilum of this organ to give rise to metastasis.

Up to this point there is no difference of opinion regarding the technique to be applied. The case becomes different, however, when we consider to what extent resection of the stomach is to be carried out: whether in cases of cardial carcinoma one can limit oneself to partial resection of the stomach, or whether one should always perform total gastrectomy, and also whether one should at the same time sacrifice a large portion of the pancreas, so as to remove the glands on the upper rim of this organ. The latter view is strenuously defended by Allison and Borrie (1949). They base their conviction entirely on the results of an anatomical examination, and they are of opinion that radical removal of the tumour can only be effected by complete removal of the stomach, the spleen, and a large part of the pancreas. I cannot share their view, for experience teaches us that metastasis in lymphatic glands is mostly limited to the paracardial group of glands, and the glands along the left gastric artery. When the glands on the upper rim of the pancreas are affected, we shall nearly always find metastasis at the same time in lymphatic glands that cannot be removed together with the tumour. Therefore I cannot admit that the way in which the tumour propagates would justify such a comprehensive operation in all cases, although I am prepared to admit that extension of the tumour has compelled us in a small minority of the cases to proceed to total gastrectomy. In this group there were 12 cases of cardial carcinoma where we performed total gastrectomy. We must add that the mortality attending the latter operation is considerably higher than that for partial gastrectomy for cardial carcinoma. In the group published by Allison and Borrie the mortality of total gastrectomy was 29%; the corresponding figure in our Utrecht Surgical Department is 20% for all cases of total gastrectomy; for the small number of cases of total gastrectomy for cardial cancer it was 8·3%, while mortality after partial gastrectomy for cardial carcinoma came to slightly more than 15%. In conclusion it cannot be denied that total gastrectomy causes very serious changes in the digestive process, and it may lead to grave disorders in certain patients. I am, therefore, of opinion that, if it is at all possible, without raising the direct and the late mortality of this operation, a portion of the stomach should be retained.

With an occasional exception all the patients who were sent to us underwent an operation, even those in whose case we could reasonably assume that the tumour was inoperable. In these cases our object was always to make swallowing possible again. The distressing condition of these patients, who without artificial means must die from starvation, justifies every attempt. Great age or bad condition were in themselves not contra-indications.

[Here Professor Nuboer went into the details of the biochemical investigation and preparation for operation.]

The technique of the resection of œsophagus and cardia has been amply described on several occasions. As I mentioned already, the technique applied by us differs in several respects from that described by Adams and Phemister (1938), Sweet (1952) and others.

As the tumour is likely to extend in the direction of the lesser curvature, it will become desirable to remove not only the cardia and the fundus of the stomach together with the lymphatic glands of that region, but also the entire lesser curvature (Figs. 1 and 2). When along the greater curvature a strip of the stomach is left, then after the wound of the stomach has been sutured a tube is formed, the diameter of which is about equal to that of the œsophagus. The resection of the stomach is performed by us with the help of the von Petz instrument, which enables us to perform this part of the operation very rapidly (Fig. 3).

After the amputation of the œsophagus well outside the tumour, and of the top of the gastric tube it is very simple to make an end-to-end anastomosis between them. The tube may be given any desired length; the anastomosis may even be effected above the aortic arch, the stomach tube being moved upward behind the aortic arch (Fig. 4).

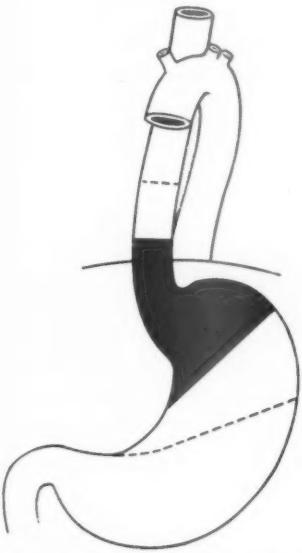

FIG. 1.—Extent of resection of œsophagus and stomach in cardial carcinoma.

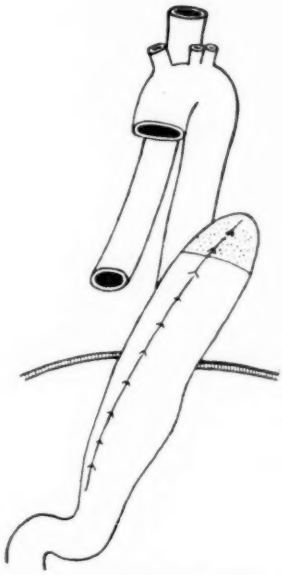

FIG. 2.—The stomach tube is formed. (The top is mostly not well vascularised.)

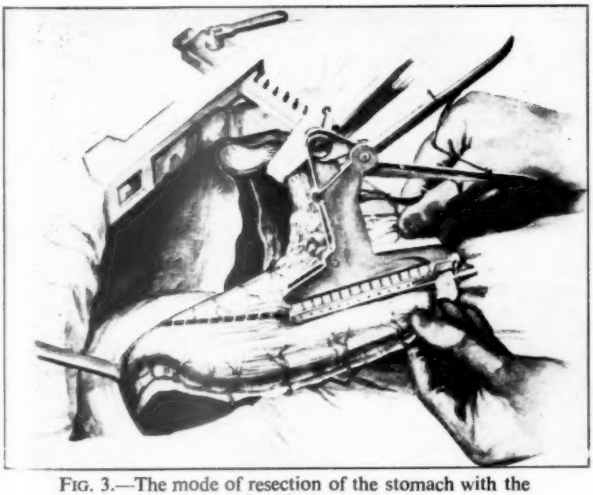

FIG. 3.—The mode of resection of the stomach with the von Petz instrument.

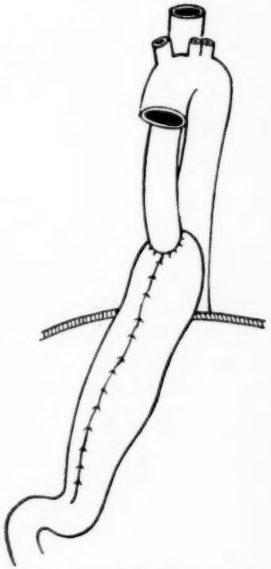

FIG. 4.—End-to-end anastomosis is performed between œsophagus and stomach tube.

This technique offers several advantages. To begin with, all the glands along the left gastric artery and those along the lesser curvature of the stomach are removed. Further, the organ obtains a shape to enable it easily to be brought into the mediastinum, covered by the mediastinal pleura. Even when the anastomosis must be raised above the aortic arch, the stomach tube is moved in its entirety into the mediastinum, and placed behind the aortic arch. Finally, this technique reduces the acid-producing portion of the stomach considerably; the consequence is that we have never observed peptic œsophagitis or peptic ulcers of the œsophagus after performing this operation for carcinoma. Cicatricial stenoses, moreover, if they occur, and this is very rare, may be stretched at one dilatation.

Post-operative measures aim first of all at the early expansion of the left lung. After the operation a drainage tube is introduced into the thoracic cavity, and suction takes place at a tension of about 30 cm. water. The tube is removed after forty-eight hours. Nutrition is administered parenterally only for three or four days: a glucose solution is slowly fed by means of an intravenous drip. The greatest care should be exercised in the case of older patients. On the third or fourth day we attach a drip-feed to the nose-tube, which in the course of the operation is always placed through the anastomosis as far as the duodenum; by means of this drip-feed we administer a solution of amino acids with glucose. On the fifth day after the operation feeding *per os* commences; at first only fluid nutrition is supplied, but gradually it becomes more and more solid. We should not omit to say that during five post-operative days we administer penicillin and streptomycin; the dosages are respectively 500,000 units and 1 gramme daily.

In connexion with an investigation of protein metabolism after operations, a number of patients were at an early stage and via a nasal tube supplied with a diet containing a large percentage of proteins and fats; it was our intention to provide the patients with plenty of materials for the healing of the wound, and at the same time to improve the nitrogen balance. Our experience has not been particularly favourable. Nearly all the patients had difficulty with the diet, but the reason was obscure, until on the fifth day one patient developed symptoms of acute pancreatitis, from which he succumbed. In my opinion it is not impossible that in this case (and the others) the diet that was administered taxed the digestive glands excessively, especially owing to the large quantities of fats, which caused a feeling of discomfort. Solutions of amino acids and glucose were tolerated well from the beginning.

The same therapy was applied in cases where total gastrectomy was found to be necessary.

As I have already said, in all cases where for technical reasons resection was possible the tumour was removed, even when metastasis at some distance was present. Removal of the tumour yields the best palliative results; not only because the capacity for swallowing is restored, but moreover because the large ulcerating tumour, which unceasingly causes loss of blood and proteins, is removed. After palliative resection the patients live for a comparatively long period in fairly comfortable conditions, and death is caused by metastasis at a distance. Local recurrence in the anastomosis was observed on two occasions.

In the past, when resection was impossible for technical reasons, we performed gastrostomy or jejunostomy. This is open to serious objections, however. Its mortality is high, and the patient remains in a miserable condition, for he is not able to swallow. Of late years, therefore, we gradually did more and more anastomoses. In some cases it is possible to mobilize the fundus of the stomach to such an extent that above the tumour a connexion may be made between œsophagus and fundus. We performed this operation on 6 occasions, but it is not so satisfactory as œsophago-jejunostomy.

The latter operation was done eleven times: we mobilized a coil of the jejunum according to Roux, and it was anastomosed to the œsophagus at some distance above the tumour. These anastomosis operations yield excellent results; they enable the patient to swallow to the end of his life. Out of 17 patients who underwent these anastomosis operations we lost only one, owing to hyperpyrexia.

In a fairly large number of cases it is not possible to perform this operation, because there exists extensive metastasis in the peritoneum, or because the diaphragm has to a large extent been infiltrated by the tumour. Of late we have on some occasions inserted a Souttar's tube, with satisfactory results.

149 patients were admitted to the University Surgical Department at Utrecht on account of carcinoma in the region where the œsophagus merges with the stomach; 147 of these underwent an operation. Our selection was as ample as possible, as it was our intention to restore the passage through the digestive channel, even if there was only a remote possibility of success. In 90 cases resection was done, on 12 occasions the stomach was totally extirpated, with a mortality of 8·3% and in 78 cases we performed partial resection of stomach and œsophagus with a mortality of 15·4%. The last-mentioned operation was in 55 cases performed with curative intentions (10·9% mortality), and on 23 occasions it had only a palliative character, as metastasis at a distance was present in the liver or elsewhere (26·1% mortality) (Table I).

TABLE I.—OPERATION MORTALITY FOR THE DIFFERENT GROUPS OF PATIENTS WITH CARCINOMA OF THE CARDIA

| Nature of operation | Number of patients | Died | Percentage |
|---|---|---|---|
| Curative resections of cardia and œsophagus .. .. .. | 55 | 6 | 10·9% |
| Palliative resections of cardia and œsophagus .. .. .. | 23 | 6 | 26·1% |
| Palliative total stomach resections in carcinoma of the cardia .. | 12 | 1 | 8·3% |

The tumour was removed in 77 male patients, aged from 36 to 80, and in 13 female patients, aged from 43 to 70. When the mortality statistics of the different age groups are studied (Table II), it will be seen that the risks of the operation increase only slightly with age. It is important to note that a somewhat large number of patients belong to the higher age groups, for 33 out of the total were over

TABLE II.—OPERATION MORTALITY IN DIFFERENT AGE GROUPS IN 90 PATIENTS FOR WHOM STOMACH AND ŒSOPHAGUS RESECTION WERE DONE FOR CARCINOMA OF THE CARDIA

| Age groups | Number | Died | Percentage |
|---|---|---|---|
| below 40 years .. .. .. .. .. .. .. .. | 4 | 0 | 0% |
| 40–50 years .. .. .. .. .. .. .. .. | 10 | 1 | 10% |
| 50–60 years .. .. .. .. .. .. .. .. | 28 | 5 | 17·9% |
| 60–70 years .. .. .. .. .. .. .. .. | 31 | 4 | 12·9% |
| above 70 years .. .. .. .. .. .. .. .. | 17 | 3 | 17·6% |

65 years of age. It goes without saying that we are not justified in drawing far-reaching conclusions from this comparatively small number of cases, but one gets the impression that for all the age groups the risk differs very little. This is an indication that the age factor need not be a bar for this severe operation, and that it may be indicated for older persons also, provided pre-operative and post-operative treatment is very good. Out of 90 patients who underwent this operation 13 died immediately afterwards (Table III). When we cast our eye over the causes of death, it is conspicuous that 7 out

TABLE III.—CAUSES OF DEATH AFTER PARTIAL OR TOTAL RESECTION OF STOMACH AND ŒSOPHAGUS FOR CARCINOMA OF THE CARDIA

| | | | |
|---|---|---|---|
| Pulmonary embolus | 1 | | |
| Shock (hæmorrhage) | 1 | Cardiovascular disturbances .. .. .. | 7 |
| Pulmonary œdema | 1 | | |
| Cardiac insufficiency | 4 | | |
| Cerebral hæmorrhage or embolus .. .. .. .. .. .. .. .. | | | 2 |
| Empyema thoracis due to failure of anastomosis .. .. .. .. .. .. .. | | | 2 |
| Acute pancreatitis .. .. .. .. .. .. .. .. .. .. .. | | | 1 |
| Peritonitis (without obvious cause) .. .. .. .. .. .. .. .. .. | | | 1 |
| | | Total | 13 |

of 13 patients died of cardiovascular irregularities, 2 died of cerebral hæmorrhage, only 2 died of sutural insufficiency, 1 died of acute pancreatitis and one of peritonitis without obvious cause. We may assume that the greater age is partially responsible for the death of 5 patients who succumbed to cardio-vascular trouble, and the 2 who died of cerebral hæmorrhage.

Out of 55 patients who underwent curative resection 49 stood the operation. Out of 20 patients who were operated on five or more years ago, 7 are still alive; this means a survival of 35%. It must be remembered that a number of the patients who died in the meantime did not die of carcinoma; they were in the main old persons who died of some intercurrent disease. This would tend to show that carcinoma of the cardia may be looked upon as one of the least malignant carcinomas of the gastro-intestinal tract, and it is therefore important to point out that an early diagnosis is of the very greatest consequence.

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**Mr. P. R. Allison** (The General Infirmary at Leeds): Carcinoma at the cardia may be found to be either a squamous carcinoma of the œsophagus secondarily invading the stomach, or a primary glandular growth of the stomach spreading upwards into the œsophagus, but the title of this discussion limits the consideration to the latter group. This is an important distinction, for, although many of the problems are the same or similar whatever the point of origin of the growth, the statistics would be altered by the inclusion of primary œsophageal lesions.

A carcinoma starting in the cardiac end of the stomach may remain "silent" for a long time, or there may be slight indigestion, loss of energy, loss of weight, anæmia or bleeding. These symptoms may, however, occur from a relatively simple cause and they may not be pronounced enough to lead to investigation. If suspicions are aroused, a routine radiological examination of the stomach is the most that is usually carried out. Even the radiologist may miss the lesion unless he examines the mucosal folds with small amounts of barium in various positions. The most menacing symptom is dysphagia, but this may be slight and transient in the beginning, so that both patient and doctor may be falsely reassured by the absence of difficulty after a few meals or a few days. When an abnormality is seen on the radiograph, its accurate interpretation may not be possible by this means alone, for similar pictures may be given by a simple gastric ulcer or by cardiospasm. Great experience of œsophagoscopy

is necessary to detect the slight change of resistance or the unexplained deviation of the channel of entry into the stomach that may be produced by an early carcinoma that is itself out of sight. The immediate environs of the cardia are the least visible to the gastroscopists also, so that, in order to make a tentative diagnosis in the patient with early disease, it may need the careful assessment of many pieces of evidence, each of which by itself is inconclusive. Finality is not always achieved until the tissue is under the microscope, but, so long as the operative risks are not prohibitive, it is perhaps better to perform a gastrectomy for what turns out to be a simple lesion than to watch each patient until he has an obvious, but inoperable, carcinoma. Particularly is this so at the cardia, for simple gastric ulcers in this area are notoriously difficult to heal, show a strong inclination to recur and are, in the minds of most surgeons and pathologists, less certain to remain simple. Healing of such a simple ulcer with dense scarring has been seen to produce œsophageal occlusion, but this is a rare event.

When a diagnosis has been made, a peritoneoscopy is a useful pre-operative measure. Although the information from this can never determine with certainty that the lesion is operable, it may sometimes demonstrate secondary deposits in liver or peritoneum and so save the patient from a futile laparotomy or abdominothoracic exploration. The peritoneoscopy can be done at the same time as the œsophagoscopy under intravenous anæsthesia if the rest of the evidence suggests that the patient is worth considering for surgery. Such points of economy in time and labour are of the greatest importance to both surgeon and patient.

The careful pre-operative preparation of these patients is such as should be carried out for all those who are to undergo a major operation. Oral hygiene is important, not only because of infection of the respiratory tract but also for the avoidance of mediastinal contamination at operation and for good healing of anastomoses afterwards. Teeth are important for proper eating after operation and are therefore only removed if they are beyond cleaning. Such dental treatment as may be necessary can be carried out under the same anæsthesia as is used for the œsophagoscopy, but if this entails extractions the patient is warned beforehand and consent obtained. Only if the lesion is thought to be operable are dental measures carried out. Two weeks must be allowed for the mouth to be clean after dental extraction, so it is important to do this early in order to avoid delaying the main operation by a series of consecutive minor operations and investigations. If a proper recovery room is available, all these things can be done in the outpatient department. If a patient has œsophagoscopy, peritoneoscopy and dental extraction at the same time, he may be kept in hospital overnight, but not necessarily so. The use of the outpatient department for these measures is worth stressing, for it prevents the beds being filled with patients being investigated or for whom nothing can be done, and so decreases the time spent on the hospital waiting list of those patients who can be treated. Even when the patients can swallow solids they are given a high protein high vitamin fluid diet in order to reduce trauma, stagnation and infection. Whatever the blood count may be a transfusion of two pints of blood is given five or six days before operation, and it is a matter of clinical observation that this does more good than can be assessed or appreciated by chemical observations. For two days before operation a non-absorbable sulphonamide cream is given by mouth and a mega unit of penicillin intramuscularly. The patient arrives in the anæsthetic room with a Ryle's tube in the œsophagus which is aspirated and withdrawn immediately before the induction of anæsthesia. Œsophagoscopy and toilet are performed and a Tampax pack left in the œsophagus just below the cricoid cartilage.

The surgical problems can be considered under four headings:

(1) The relief of obstruction.
(2) Excision of the growth and its extensions as one continuous block of tissue.
(3) Restoration of continuity of the alimentary tract.
(4) Post-operative maintenance of normal metabolism and blood formation.

It is important that the first three of these should be achieved in one operation and the author's personal preference is for the use of one incision. It is important that the particular object of the operation should be kept clearly in mind so that the magnitude of the trauma should be related to the success achieved. The lessons that appear to have been learnt from the present series are, firstly, that in the treatment of carcinoma of the stomach, post-operative morbidity is more important than operative mortality; secondly that an attempt at cure should be radical according to the known anatomy of cancer extension; thirdly that palliation should bring physical and mental relief to the patient with the least possible suffering and not merely a feeling of relief from responsibility on the part of the surgeon, and fourthly that the unknown biological factors in carcinoma put prognosis almost on the same level as gambling.

### *The Palliative Relief of Obstruction*

The Souttar's tube that is so valuable in carcinoma of the œsophagus has very rare application to obstruction of the cardia by gastric growths and can be a danger. The infiltration of the gastric wall may so fix the greater curvature that the tube may perforate this and enter the peritoneal cavity.

Gastrostomy or jejunostomy does not relieve the obstruction and these operations have nothing to recommend them except as an escape for the surgeon. When the primary growth can be removed resection with œsophago-gastrostomy or œsophago-jejunostomy may be performed, but if the lesion is fixed and irremovable œsophago-jejunostomy above the growth is well worth doing. Palliative

resection and œsophago-gastrostomy for primary carcinoma of the stomach invading the œsophagus has only been performed on 6 patients in this series. Of these 3 died from their operation from sloughing of the stomach, embolus and liver necrosis, and the 3 who survived lived for six months, six months and two years respectively.

Palliative resection with œsophago-jejunostomy cannot be separated in this series from the attempted curative operation, for this leaves too much room for surgical equivocation. A very high proportion of the lesions treated by resection and œsophago-jejunostomy were so advanced (and paintings of them all are in the records) that the operation could hardly be classed as more than palliative. That some of these operations turned out to be unjustified is admitted, but lessons have to be learnt, and in fact one or two that were tempting to leave behind have lived for five or six years.

Palliative œsophago-jejunostomy by Roux loop without resection of the growth has been performed on 30 patients. These have certainly brought relief to patient, relatives and doctor. The operation seems to have established itself as a useful measure in certain selected circumstances.

*Excision of the Growth and Its Extension*

As carcinoma of the stomach has no respect for anatomical boundaries, the surgeon must be equally ready to transgress them in its treatment. The resection of the growth with a margin of normal tissue, together with the cellular and lymphatic tissue concerned in its immediate drainage, must be the aim here as elsewhere. There is now ample histologic evidence that malignant cells spread in the lymphatic plexuses of the stomach without regard to the shaded areas of drainage so often displayed on diagrams, and there is growing support for the belief that operable carcinoma of the stomach should be treated by total gastrectomy. The spread up the œsophagus is often much higher than can be detected by palpation and a minimum of 2 in. (5 cm.) of apparently normal œsophagus should be removed. The mediastinal cellular tissue including that of the lateral pulmonary ligaments, the hiatus of the diaphragm, the retroperitoneal tissues down to and including the body of the pancreas and spleen, the splenic and left gastric arteries at their origin from the cœliac axis should all be resected in one piece together with the stomach and lower œsophagus, and the great and lesser omenta. If the left lobe of the liver or the suprarenal capsule is involved by direct spread of the growth, it should be resected in continuity with the rest of the mass. It is needless to re-state here the convincing support that anatomy and pathology have given to this wide block dissection. It is not a shocking operation and is carried out in cellular planes with the minimum loss of blood.

*Restoration of Continuity*

If the above resection is performed, there is very little choice in the matter of restoration of continuity for the stomach has gone, and a loop of jejunum will not reach the œsophagus to the level at which it has been resected. The œsophagus must therefore be anastomosed either to a loop of jejunum fashioned on the Roux principle or a segment of colon must be swung up. The author has no experience in the use of the colon for this purpose.

It is opportune here to state the disadvantages of the operation of œsophago-gastrostomy:

(1) The spread of carcinoma in the lymphatics of the stomach makes it likely that malignant tissue is left behind in the stomach wall.
(2) The anxiety of the surgeon that the œsophagus and stomach tube should meet easily makes him liable to cut close to the growth both in stomach and œsophagus.
(3) The liability to local recurrence and dysphagia which is dependent on (1) and (2).
(4) The morbidity from reflux œsophagitis.

Of 25 œsophago-gastrostomies performed by the author for malignant disease at the cardia in patients who lived long enough for their morbidity to be assessed, 20 had dyspepsia ranging from slight to severe, 22 failed to gain weight, 8 developed dysphagia from stenosis of the œsophagus due to reflux peptic ulceration (and 1 of these died four years after operation from perforation into the pericardium), and 3 developed recurrent carcinoma at the site of anastomosis, from which they died. One patient who survived operation for nine and a half years is still alive "after much suffering patiently borne" but the suffering has been shared by the rest of the household.

Œsophago-jejunostomy by inverted U leads to resection of the œsophagus too low and is not free from alkaline œsophagitis even with a large entero-enterostomy.

The author's choice is therefore œsophago-jejunostomy by Roux loop, but there is room for further research to determine whether the loop should be completely isolated and anastomosed above to the œsophagus and below to the duodenum, or whether it should be left in continuity and the duodenum used as a bile and pancreatic duct coming in at the side of the loop. In this series the latter method has been used. This type of restoration is not free from morbidity, but post-operative symptoms are mainly controllable. The patients do need medical care.

*Post-operative Maintenance of Normal Metabolism and Blood Formation*

Post-operative "dumping" may occur as after any other gastric operation, but it is not more frequent than after partial gastrectomy, tends to improve after a few months and is amenable to treatment. Diarrhœa may be present for a short time, but rapidly clears up. The patients are always more liable than the normal person to loose stools as a result of infection, too big meals or hasty

eating. Some degree of steatorrhœa is nearly always present but is much more likely to be present, as indeed are the other symptoms, when the operation has been performed for advanced disease. The onset of uncontrollable symptoms has always been a warning of rapid recurrence of the carcinoma. A secondary anæmia, or, after four or five years, a macrocytic anæmia may develop.

Pulmonary tuberculosis is an important possible complication in those patients who have been starved for long, and whose economic and social conditions are unsatisfactory.

The doctor of every patient is provided with the following instructions as the patient leaves hospital:

*Rules for Patients with Œsophago-jejunostomies*

1. Small meals to be taken up to 5 a day.
2. Meals to be taken dry except for an aperitif, e.g. glass of sherry.
3. Meals to be well masticated and eaten slowly.
4. Extra food in the form of butter, cheese, milk and cream, wherever possible.
5. A liver preparation, e.g. Hepovite or Hepamino, to be taken daily, 1 drachm t.d.s.
6. If tendency to diarrhœa, hydrochloric acid dil., minims 10, to be taken in water before meals.
7. A blood count to be taken every six months, and X-ray of chest is necessary at least once a year.

If these instructions are followed, the patient should be able to maintain his weight, do his work and enjoy his life. In the author's series there have been 75 radical total gastrectomies as defined above where continuity has been restored by the Roux loop. Of these 75, many advanced growths and some involving the whole of the stomach, 22 died from their operation and 17 died from recurrence in under one year. A further 17 patients who lived longer than one year are since dead, but not all of them from recurrence of growth. The survival periods of these 17 patients are given in Table I.

TABLE I

| Survival in years | 1–2 | 2–3 | 3–4 | 4–5 | 5–6 | 6–7 |
|---|---|---|---|---|---|---|
| No. of patients | 8 | 4 | 2 | 1 | 1 | 1 |

TABLE II

| Survival in years | Under 1 | 1–2 | 2–3 | 3–4 | 4–5 | 5–6 | 6–7 |
|---|---|---|---|---|---|---|---|
| No. of patients | 2 | 4 | 2 | 3 | 3 | 1 | 4 |

19 patients are still alive and their survival times are shown in Table II.

The 4 patients who have survived between six and seven years had very cellular but well-differentiated adenocarcinoma, and the four- to six-year survivals had highly anaplastic and very invasive adenocarcinomas. It is not possible here to give details of every patient, but it is worth stressing that of the 4 survivors over six years, 1 is a coal miner who eats four meals a day, works eight hours a day and has only been off work once for a carbuncle of neck since his operation; 1 is working in a theatre, eats normal meals, has no symptoms and has never lost a day's work; 1 is a working gardener who eats anything and feels fine; and 1 has recently been off work for lassitude and has been found to have a macrocytic anæmia. The patients who do best are those that have the best wives. Those who return home to meals of tea and teacake have a problem that cannot be solved by surgery.

**Dr. F. E. Revers** (*Utrecht*) referred to the importance of hypoproteinæmia in patients with carcinoma of the stomach, and suggested that interference with liver function was a factor in its production and that probably this liver function disturbance made it very difficult to restore plasma albumin content by feeding.

**Mr. Hermon Taylor** stated that in these cases he was in favour of preserving some stomach, making a direct anastomosis between the œsophagus and the pyloric antrum.

He had found that reflux œsophagitis was uncommon despite the intra-thoracic remnant of stomach.

He favoured an abdominal exploration of the mass, the excision being extended up into the chest if conditions were favourable. If they were not, he carried out a retrograde diathermy of the malignant stricture at the cardia, after opening the stomach.

**Mr. R. H. Franklin** referred to his figures during the last three years. He had had 26 cases of carcinoma of the cardia. In 3 patients abdominal exploration only was carried out; all 3 died within three months. In 23 major explorations there were 7 operative deaths. In 20 he had done total gastrectomy with block dissection of the glands, and in 1 a partial gastrectomy; in 2 patients whose cancer arose in a thoracic stomach a resection with œsophago-gastrostomy in one and resection followed by jejuno-œsophagostomy in the other were carried out. Of 16 survivors, 8 were still alive, one two and a half years after operation. In preparation for operation he relied mainly on a fortified liquid diet, and he stressed the importance of allowing patients to take nourishment at any time without relation to normal meal times. Alcohol was also useful.

**Mr. J. Gilmour** stated that in Newcastle the incidence of carcinoma of the cardia was 12–13% of all gastric cancers, and the operability rate was just over 50%. Even then in resected specimens lymph invasion had occurred in 70% as against 40% in other gastric cancers. The outlook was therefore bad and the best results were in cases with no lymph involvement.

He stressed the importance of recognising dyspeptic symptoms, as many growths spread up to the cardia causing a terminal dysphagia. Such initial dyspepsias, 3 months to 3 years in duration, occurred in 8 of his own 15 cases, whereas only 7 had primary dysphagia.

# Section of Obstetrics and Gynæcology

President—VICTOR LACK, F.R.C.P., F.R.C.S.Ed., F.R.C.O.G.

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## Co-ordination in the Care of Carcinoma of the Uterus

By H. HARVEY EVERS, M.S., F.R.C.S., F.R.C.O.G.

*Professor of Midwifery and Gynæcology, University of Durham*

IN the course of examining in six Universities and for the Conjoint Board, I found that remarkably few candidates have examined or followed a case of malignant disease of the uterus. Worse still, as an assessor of the books of cases and commentaries submitted by M.R.C.O.G. candidates, I have noticed a gradual disappearance of these cases from the records. Disquieted by the prospect of a race of gynæcologists with little or no direct experience of this common and vital section of the specialty, I recently brought the matter to the attention of the Council of the Royal College of Obstetricians and Gynæcologists. A full enquiry is afoot, but its results are as yet incomplete and, of course, confidential. Consequently, whatever I may say here must be regarded as personal opinion, and in no way official.

The gynæcological departments of many teaching hospitals have suffered a general loss of clinical material due, no doubt, to the establishment of new Units along their lines of drainage. But this alone cannot account for the marked numerical fall in cases of malignant disease. There is reason to believe that radiotherapy departments are accepting directly cases of uterine malignancy. That this should be the case in some hospitals, both teaching and regional, where a gynæcological department functions under the same roof, seems inexcusable. In many regional hospitals the situation is further aggravated by geographical separation, sometimes wide, of the two departments. In certain regions some gynæcological units are dispersed at the periphery, while concentration of the radium supplies and X-ray equipment demands ostensibly a measure of concentration at the centre. In these hospitals, therefore, in addition to the direct acceptance of patients, there is the sinister possibility that the patient referred by the more remote regional gynæcologist to the central therapy unit may be permanently deprived of any further gynæcological contact.

In cases of corporeal cancer some measure of protection is initially afforded by the prerequisite of operative confirmation of the diagnosis. It is still not unknown, however, for menopausal or even post-menopausal hæmorrhage to be treated by deep X-ray without previous diagnostic curettage. Most cervix cases are, unhappily, only too obvious clinically, and it is almost certainly due to direct reference of these cases to radiotherapy that in some gynæcological units corporeal cancer appears, paradoxically, to be a commoner disease.

But even the most obvious carcinoma of cervix calls for a considerable degree of clinical experience and training. Accurate staging, intelligent biopsy, assessment of radiosensitivity, cystoscopy, pyelography, sigmoidoscopy, biochemistry, hæmatology and bacteriology are all essential from case to case—and not merely for the initial assessment of pathology and the design of the precise pattern of

treatment, but also for perceptive and alert follow-up. Such training and experience cannot possibly be acquired by mere external and bimanual examination—it must be supplemented from time to time by the intelligent correlation with laparotomy findings which is available only to the clinical gynæcologist.

When this principle is fully and cordially conceded, complete co-operation between gynæcologist and radiotherapist is possible and, indeed, exists in some hospitals at present. When it is not conceded, the radiotherapist accepts direct and full responsibility for treatment, the aid of the gynæcologist being sought only when some co-existing but undiagnosed concomitant pathology causes trouble, or when some subsequent complication, such as fistulæ, radium necrosis, perforation of the uterus, peritonitis, pelvic abscess, intestinal obstruction, &c., arises as the result or in the course of radiotherapy. In such circumstances the gynæcologist may find his therapeutic horizon limited to hopelessly complicated node dissections, colostomy, transplantation of ureters, and that final triumph of surgical technique over common sense and common humanity, "pelvic exenteration".

Where the principle of co-operation is partially accepted, the tendency is for the radiotherapy unit to appoint its own gynæcologist. This is specious lip-service to co-operation in that it approves direct reference of patients to the radiotherapy unit. It differs fundamentally from the scheme whereby a small hospital group of gynæcologists delegates to one of its members the task of co-operation with the radiotherapy unit in all its malignant cases. Such an arrangement may, in some circumstances, be expedient, but it is not, to my mind, ideal or even desirable. Every gynæcologist should retain personal contact with the overall care of these very important cases.

Without undue cynicism, one must not be unmindful of a further undesirable trend. In some hospitals where full and cordial co-operation at present exists this happy condition of affairs is to some extent dependent upon the radiotherapist's lack of beds—and to a less extent upon his lack of suitable facilities for independent follow-up. We must therefore regard with some disquiet the present trend towards the further development of bigger and better independent radiotherapy centres embracing full inpatient, as well as outpatient, accommodation and equipment.

Such a centre with its own specialized surgeons, gynæcologist, &c., if left to unrestricted evolution, will be liable to develop into a self-contained Cancer Hospital (so popular in America); and if patients are accepted direct, will gradually deprive all other departments of their cases of malignant disease. A number of such centres, strategically dispersed, could ultimately form a sort of Carcinoma Cartel or "cancer closed shop". As a result of the director's natural (radiotherapeutic) bias, the gynæcologist may find his clinical material limited to radiotherapy "throw-outs", and his operative field restricted to palliation and wide extirpation. These cancer gynæcologists, bringing a savage ingenuity to bear upon the task of devising bigger and better methods of evisceration, may well become a race apart—a sort of self-styled gynæcological élite with loyalties more surgical than gynæcological. Their more humble colleagues, deprived of cancer material during training, may be regarded superciliously but tolerantly as well-meaning, but not really competent to deal with the wide and more complex problem of malignant gynæcology.

But surely our specialty is narrow enough to provide our young men and women with full experience and training to all aspects of gynæcology—to produce consultants competent to handle every form of gynæcological disorder or disease. For this purpose there must be no diversion of clinical material from gynæcological departments. And to this end, we must spare no efforts to guide the evolution of these radiotherapy centres into the right channels. The problem is by no means exclusively a gynæcological one. Many other departments of medicine and surgery find themselves in the same predicament, and concerted action is obviously desirable.

I would submit for discussion the following general principles for the care of these patients:

(1) It should be clearly recognized at the highest level that cancer of the uterus is a gynæcological disease, the care of which should be entrusted primarily and throughout to the gynæcologist.

(2) The radiotherapist with his physicists, technicians and specialised appliances is an essential and welcome component of the team but, to avoid dual control, so confusing to the doctor and so prejudicial to the patient, the supreme responsibility must lie with the gynæcologist.

(3) Radiotherapy units or centres should only accept these patients when referred by gynæcologists.

(4) The gynæcologist who finds himself too remote geographically for full co-operation with the radiotherapy department, should primarily refer his patient to a gynæcologist at or near that department, thereby safeguarding subsequent gynæcological control.

(5) The primary decision as between surgery, radiotherapy, or both, should rest with the gynæcologist. Correlation between surgery and radiotherapy, whether pre- or post-operative, must be maintained.

(6) The province of the radiotherapist is to design the precise dosage, distribution, type of applicator, screenage, &c. For this purpose he should co-operate in the original assessment of the local pathology during the examination under anæsthesia at which the complete plan of treatment should be designed.

(7) The gynæcologist should, if he so wishes (and many do), personally insert the radium with the technical assistance of the radiotherapy team. The quest for that elusive internal os can be humiliating even in cases of dysmenorrhœa and infertility. In some malignant cases it can defeat both the patience and skill of an experienced operator. False passages, perforations and total failure to insert the central tube are much more likely in the hands of the inexperienced, and for these the patient pays a heavy price. In some centres this essentially gynæcological procedure is entrusted to a radiotherapy registrar.

(8) Inpatients should be accommodated in gynæcological beds or, at least, in beds over which the gynæcologist and his team can exercise some supervision and control. A few of the beds in a radiotherapy centre might be reserved for joint research.

(9) Follow-up should be a joint responsibility, and should be carried out in a gynæcological department properly equipped and staffed for this intimate type of examination. There is much to be said for the system whereby these patients attend the ordinary follow-up clinics of the gynæcological department. Segregation of malignant cases may have undesirable effects, psychological and otherwise.

(10) The undergraduate student should be given every opportunity of seeing these patients in the outpatient department, of observing their preliminary investigation, of taking part in the technical examination under anæsthesia, and of interesting himself in the after-care and follow-up. He will thereby become imbued with the paramount importance of overall gynæcological supervision, and, by the same token, will be vastly less likely after registration to refer his own patients direct to the radiotherapist.

(11) The postgraduate trainee gynæcologist must, under supervision, be afforded as much personal responsibility as possible for such cases in all phases. Such a desirable consummation can only be achieved by primary relegation of all cases to gynæcological units and by sustained gynæcological control.

Much might be said on the subject of the relative opportunities for progress and research in the two departments. I have avoided reference to "smears" and carcinoma *in situ*. Not because I think it a subject to ignore, but because I regard the issue as undecided, and highly controversial. In the hands of the fanatic it can lead to considerable cervical carnage and to more than somewhat of pelvic pillage! In more temperate hands it may well constitute a form of clinical research stimulating alike to the student and trainee, and is therefore to be encouraged with safeguards in teaching gynæcological departments. There are also many other avenues of research open only to the clinician, and calculated to widen the gynæcological horizon. This has special application to the commoner cervix cases—but there is also a wide field in the syndrome of diabetes, heredity, late menopause, radium, œstrogens, &c., in relation to carcinoma of the corpus. I find it difficult to imagine that a department like radiotherapy, concerned predominantly with the pure mechanics of treatment, can contribute much to the improvement of visibility in the gynæcological atmosphere. We must, however, watch with interest the activities of the relatively new "linear accelerator".

The basic claims which I have enumerated may seem to constitute considerable territorial ambitions —they may even savour a little of the unilateral; but if the uterus is no longer gynæcological territory, we are face to face with quite a new type of frontier. From contacts with my colleagues it is clear that feelings on this matter of co-operation are rising in temperature as well as tempo. But we must maintain an attitude of patience and tolerance—tolerance, not of what would be prejudicial to our patients and our specialty, but of reasonable compromise and co-operation. I would plead for no appeasement—and no retreat from the principle of overall gynæcological control.

## DISCUSSION ON RUPTURE OF THE UTERUS IN PREGNANCY AND LABOUR

**Mr. Donald Fraser:** Cases of ruptured uterus in pregnancy or labour are dangerous and bristle with difficulties of diagnosis and treatment. My own experience is limited to 5 cases—3 in relation to previous Cæsarean sections or hysterotomy and 2 so-called "spontaneous ruptures". I make no apology for the paucity of this material, for too easy a familiarity with this subject is unbecoming, as many cases are preventable. This was certainly true of 2 of mine. All 5 patients survived with 2 babies and 1 uterus salvaged.

I would like to give you my impressions of current literature and to report 2 cases of rupture in pregnancy in some detail. I have not gone back very far into the literature as the quality of material and conclusions to be drawn have altered considerably over the years with modern changes in obstetric trends—notably the improved safety of lower segment Cæsarean section as a by-pass to all the gross mechanical difficulties experienced in labour.

The incidence of ruptured uterus appears to be relatively constant at about 1 in 1,500 to 2,000 deliveries. It has been estimated as the cause of maternal death in 5% of cases in the United States. In the Rotunda practice (1948–1952) 15 ruptures occurred in 20,000 deliveries, of whom 4 died. This constituted 8% of their total maternal mortality of 48 cases in that series. Various suggestions as to classification have been made and I think the most useful is that of Brierton who reported on a series of 57 cases in 1950. His groups are (1) post-Cæsarean; (2) so-called "spontaneous"

rupture; and (3) traumatic rupture. To these might be added rupture in early pregnancy usually due to criminal interference. In modern practice the first group is by far the largest and the third group, of which I have no experience, will in due course largely disappear. Cases in this third group occur only in labour and are nearly always related to gross obstetric interference—internal version and extraction notably in relation to transverse lies and placenta prævia as well as high forceps and the abuse of forceps and also ill-advised use of oxytocic drugs in labour. Many of the manœuvres leading to rupture in this group may now be regarded as obsolete or obsolescent, but the modern obstetrician with his high disregard for the difficulties of his predecessors may remember that in avoiding these difficulties by Cæsarean section he is, of course, contributing to the material of the first group and the cynic might say that he is transferring his ruptured uteruses from one statistical table to another.

The first group—post-Cæsarean rupture—now constitutes at least half and perhaps more of all cases. Extensive series of deliveries after *lower segment* operation show that the danger is not thereby eliminated, although it may be reduced. Lawrence (1949) reported 121 vaginal deliveries after previous lower segment operation, of whom 2 ruptured. Wilson (1951) reported 15 ruptures in over 900 cases; the majority were classical, but there were 4 lower ruptures. The incidence seems to be about 2% irrespective of site of operation, but there is a definite impression that the classical scar is more dangerous in pregnancy. Brierton (1950) reported 7 cases in 246, of whom the majority had had lower segment operations; 4 occurred in the classical group (94) and 3 after the modern operation (152).

Summing up, the lower segment scar is safer than the classical particularly in pregnancy—if it ruptures it tends to do so in labour—and there is a further impression that a transverse scar is safer than a vertical one. But the point still stands that a scar is not as good as the thing it replaces and it behoves us to look to our indication for the *first* Cæsarean section.

In the so-called spontaneous group, the rupture more commonly involves the lower segment and it is unusual for the corpus alone to be involved. In many of these cases there is a history or a finding of previous damage to the uterus, notably scarring in relation to previous septic abortion, scars of cervix and lower segment from previous delivery and even myomectomy. Most of the ruptures occurred again at or near term and in the majority the patient was thought to be in labour. Maternal and fœtal mortalities in Brierton's cases were: Group 1, 3·8% and 46%; Group 2, 47·6% and 85·7%; Group 3, 80% and 80%. These figures are the main justification for the rather awkward classification and they show the relative safety in the first group where the labour is probably being conducted in optimal conditions.

*Diagnosis.*—The majority of the first group are in labour at the time of rupture. This is also true of the second group and, of course, it is the rule in the third group. There is a fallacy here for the pain of rupture is often misinterpreted as the onset of labour. Abdominal pain and local tenderness are the most reliable findings often with shock. The patient may come out of labour and she may bleed excessively *per vaginam*, but these are less reliable findings statistically.

*Treatment.*—Once the diagnosis is made the actual case requires abdominal exploration with coincidental blood transfusion and the detail of operation will depend upon the local findings. Hysterectomy rather than conservation of the uterus appears to be commonplace in the literature. Some of the cases in the traumatic group where the rupture is confined to the lower segment may be conservatively treated by packing. The real treatment, of course, ought to be prophylactic wherever possible, but it would be a bold man who would suggest, at least in this country, repeat Cæsarean section in all cases, particularly if the original indication is non-recurrent. This would not avoid some of the ruptures in pregnancy, but, if it were done at 38 weeks, would eliminate a lot of these and naturally all those occurring in labour. Many American authorities make no bones about it and regard a previous section as an indication for a repeat operation. This might be modified with advantage to a dictum of "once a classical, always a section at 38 weeks" and, possibly, the patient hospitalized for some time before. If vaginal delivery is decided upon the case must be conducted in proper surroundings by people who are aware of the subtleties of uterine rupture, and even after successful vaginal delivery the uterus should be manually explored. There are some features about the previous section which make a repeat advisable—notably, previous post-operative sepsis. One of my patients had the clinical equivalent of this. She had had a non-septic hysterotomy at 24 weeks in Malaya for toxic hyperemesis after 4 normal deliveries of large babies up to 9½ lb. She must have been very ill at the time of hysterotomy as she had an extensive peripheral neuritis, signs of which persisted. She had no ankle-jerks or knee-jerks when I saw her two years later and a patch of anæsthesia on the front of her left lower leg with some extensor wasting. She had a large pelvis so I decided to conduct her sixth labour naturally and did so successfully. I was present throughout all stages of labour and for an hour later. She collapsed six hours after labour with extensive intra-abdominal hæmorrhage and I found the classical scar of hysterotomy completely ruptured at operation. She was treated by subtotal hysterectomy. She must have been starving at the time of her previous hysterotomy and I would have done well to deliver her by section. Failing that, I should have explored her uterus after delivery, although there were no adverse signs at any stage.

Another case had had a Cæsarean section, classical, with a large stillborn fœtus after a failed trial labour. We decided to deliver her at St. Bartholomew's conservatively as she had a large pelvis and the

head was engaged. After a few hours in labour with an excessive show from the beginning, she developed a suprapubic bulge and went out of labour. Although I was operating within twenty minutes of the rupture, the baby was lost and the uterus was split from the fundus down to and into the vagina with considerable bleeding behind the bladder. The dead baby had left the uterus and the placenta was attached to the scar. I had every intention of saving this uterus when I started the operation, but decided against it for technical reasons and again performed a hysterectomy. She lost both her babies, therefore, and her uterus all for lack of clinical judgment. I think she should have had a repeat Cæsarean section on her bad history. This was not a case in which to take a risk and I regard both these ruptures as preventable.

Details follow of the two ruptures in pregnancy. They are both unusual as they were corporeal ruptures following previously unsuspected trauma.

*I.*—Mrs. P., aged 28, had been attending a midwives' clinic in what was stated to be her first pregnancy. At 30 weeks, on 13.10.49, she woke from sleep at 4 a.m. with generalized abdominal pain, most marked in her groin, and she was sick. Nine hours later she was admitted to the City of London Maternity Hospital with pulse 80-90, blood pressure 110/80. She looked ill, complained of abdominal pain and the abdomen was tense with tenderness in the loin and both iliac fossæ. The fœtal heart was not heard, the cervix was closed and she had a trace of albumin in the urine specimen. She was seen by two of my obstetric colleagues, judged to have a concealed accidental hæmorrhage and treated with morphia and pethidine. She continued to be sick, an intravenous drip was set up and she was given saline followed by blood. At seventeen hours she was still being sick, her pulse was 130 and her blood pressure 130/92. The patient passed a very uncomfortable night despite heavy sedatives and large amounts of bile-stained fluid were aspirated as she had an ileus.

I saw her at thirty hours with a temperature of 100° F., pulse 130, blood pressure 130/88, pulse of poor volume. She had a third-stage peritonitis with distended, silent abdomen and, as she seemed to be losing ground, I decided to operate with no very clear diagnosis.

At laparotomy with coincidental blood transfusion there were several pints of blood in the peritoneal cavity with fœtus and placenta lying free. The uterus was contracted, even involuted, in the pelvis and there had been a fundal explosion through an irregular, thin scar. I was impressed with the patient's poor condition and did a subtotal hysterectomy. She had 3 pints of blood and 4 of saline in the next thirty-six hours. She made an uninterrupted recovery and went home in a fortnight.

We learned later that in September 1948 she had a self-induced abortion at 3 months, using a syringe. She had been admitted to hospital and the uterus explored as an incomplete abortion. There had been considerable bleeding and the uterus was packed. She developed peritonitis with paralytic ileus and was thought to have salpingitis, from which she recovered without operation.

*II.*—Mrs. J. B., aged 34, with a history of appendicectomy eighteen years before and a normal delivery nine years previously. She had a curetting six years before for menorrhagia. On 5.10.52, at 29 weeks, she was admitted to hospital at 2.30 p.m. The history was that she had had pain for forty hours, starting in the right groin, and that she had been sick. The midwife thought she was in labour, but as there was no progress finally sent her in. She was not shocked, pulse 95, temperature 98·4° F., blood pressure 126/66. The abdomen was tense, the fœtal heart was not heard, the fœtus was lying obliquely and there was a lump on the side of the uterus to the right which I took to be a fibroid. The cervix was closed, there was no show and she was not in labour. Again the diagnosis of concealed accidental hæmorrhage was made and she was given morphia. In a few hours there was no improvement in her condition, in fact she had deteriorated considerably despite a 3-pint blood transfusion. The pulse ranged from 112 to 120, the blood pressure was 88/60. The abdomen was more tense and finally dull in the loins.

At forty-eight hours I operated and found a 4-in. rent in the uterus with fœtal foot and placenta presenting. The rupture started at a depressed scar near the insertion of right round ligament and extending across the fundus. The fœtus was extracted and the excised scar sewn up in three layers. She had three further pints of blood. Her convalescence was disturbed by collapse of the right lower lung, but she went home in good order on the sixteenth day with hæmoglobin 80%.

Detail of the previous curetting from another hospital did not yield any useful information. Her convalescence had been uneventful at that time. Two months later she had made a complete recovery, having had one normal period.

Both these cases had previously unsuspected uterine damage and I do not think it is entirely a coincidence that they both ruptured spontaneously at about 30 weeks. It is startling, at least to me, that uterine perforation at curettage should later result in rupture of the uterus. I can imagine that there must be many people who have perforated the uterus and I hazard a guess that their concern for the patient has been immediate rather than remote.

I had considered re-excising the scar on the patient whose uterus I conserved, but I have abandoned the idea and in a future pregnancy I propose to admit her at 28 weeks and do a set section at 38 weeks if things go well.

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**Mr. David M. W. Maxwell:**

*Introduction.*—I would like to include one case of rupture of the uterus associated with criminal interference and one with therapeutic termination of pregnancy. Including the ruptures in labour, I have had personal experience of 10 cases of different types in the last twenty-five years in the Windsor Area where the present population is about 230,000 and where there are 75 gynæcological beds and 120 active maternity beds. Dugger (1945) of Philadelphia described 105 cases in the last trimester of pregnancy during a ten-year period. The incidence was one in every 3,029 births. 25·8% of these ruptured during pregnancy. 84·6% of the total number (65) were considered preventable deaths in the opinion of the Committee of Maternal Welfare of Philadelphia County Medical Society.

*Case I.*—The first case comes under the heading of spontaneous incomplete rupture of the uterus with severe intraperitoneal bleeding and was operated on just prior to complete rupture resulting in a living child and mother (*see* Henderson and Maxwell, 1952).

*Case II.*—In the second case there was a clear history of criminal interference on three separate occasions. Examination revealed a gross condition of general peritonitis with tenderness and marked rigidity extending up to both costal margins.

The abdomen was opened and large quantities of pus were found and a large perforating wound of the pregnant uterus through which it was possible to pass a finger.

This was sewn up and the abdomen drained. Under the same anæsthetic the retained products were removed *per vaginam.*

Recovery was quite unexpectedly uneventful with large doses of Prontosil.

*Case III.*—This comes under the heading of accidental rupture of the pregnant uterus at 14 and 16 weeks' gestation, and concerned a woman of 40 years of age. Her doctor and obstetric physician (not myself) had decided that therapeutic termination was justified for the following reasons:

Her husband was an epileptic; she had two epileptic children and one tuberculous child; she suffered from breathlessness on exertion, and on examination was very obese, and showed a pendulous abdomen and a trace of albumin in a catheter specimen of urine.

Induction of a miscarriage was attempted by the physician concerned by dilating the cervix, rupturing the membranes and removing a portion of the membranes. Later pituitrin was given.

Two days later she developed considerable pain and tenderness in the lower abdomen with a certain amount of foul vaginal loss. Later a laparotomy was performed and a rupture in the posterior wall of the corpus low down was defined and the patient suddenly died on the table. At the inquest Dr. Bernard Spilsbury confirmed that the indications for therapeutic abortion were well justified and considered that death was primarily due to myocardial changes and secondarily due to pelvic peritonitis and an infected ovum.

*Comment.*—The first of these two perforation cases is mentioned as an example where it may be more than justified to be conservative in the treatment of either certain accidents of surgery or criminal cases. The second raises in our minds some of the possible worries associated with therapeutic termination of pregnancy *per vaginam.* Many years ago I was called to a case similar to that reported by Mr. John Howkins (1952), when he so dexterously saved a woman's life. In my case portions of both small and large intestine had been damaged through an aperture made in the uterine wall in attempts to terminate a pregnancy *per vaginam.* My patient did not recover. How can these troubles be prevented? It appears that at least one teaching school in London, North of the Thames, does not hold with the use of utus paste (or aretus paste as it was called before the war). I personally do consider that it has a very definite place in therapeutic termination and can reduce the risk of this procedure.

Most of us have experienced the technical difficulties, anxieties and dangers of termination of pregnancy *per vaginam,* particularly in a primigravid patient, by emptying the uterus at one sitting—especially if the pregnancy is more than 10–11 weeks gestation.

Most authorities will agree that termination may be carried out *per vaginam* up to 12 weeks. Thereafter it may become progressively dangerous in the primigravida and abdominal hysterotomy should be performed—preferably through a curved incision in the lower portion of the uterus so as to minimize the risk of intestinal or other adhesions forming later. Others have confidence in utus paste.

*Case IV.*—The girl concerned was primigravid and aged 23, some 34 weeks pregnant, and was admitted to King Edward VII Hospital in December 1948. About half an hour before she had been on the deck of a motor launch approaching a closed lock gate. Suddenly she was crushed between the bridge of the lock gate and the roof of the cabin of the launch (*see* Elias, 1950).

*Comments.*—De Lee, Ley and Hosking all describe accidents of patients who either fell or sustained severe abdominal blows all resulting in frank rupture of the pregnant uterus. In their cases twenty-eight hours, two days, and eighteen days respectively after the accidents operations were performed. In De Lee's case subtotal hysterectomy was performed with recovery. In Ley's case suture only with recovery ensued. Hosking's patient, in his opinion, was too ill to allow of hysterectomy and the rent was exposed and packed. The patient was up and about one month later.

*Prophylaxis and treatment.*—This matter is largely concerned with the care and skill of the operator in cases of therapeutic abortion which have already been covered by Mr. Howkins (1952) and the use of uterus paste in therapeutic abortion can also be considered. In addition the greatest care should be taken in all cases of manual removal of any placenta.

As regards active treatment, when actual rupture has occurred prompt attention to the shock and hæmorrhage before, during and after operation is always indicated. Whole blood transfusion is imperative. This must be followed by laparotomy and repair of the rupture or hysterectomy which in many cases can be permitted to be supravaginal. Later the prevention of infection in these critically ill patients is essential since they may survive the intermediate shock and blood loss only to succumb to infection later.

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**Mr. D. M. Stern:** *Rupture of the Cæsarean Section Scar in Subsequent Pregnancy and Labour*

On May 6, 1920, Sir Eardley Holland gave his classical paper on "Rupture of the Cæsarean section scar in subsequent pregnancy or labour" before a Conjoint Meeting of this Section of the Royal Society of Medicine with the North of England and Midland Obstetrical and Gynæcological Societies (*Proceedings*, 1920, **14**, Sect. Obstet., 22). In those days, of course, Cæsarean section was less common than it is to-day. The indications for its use were restricted. The maternal mortality was higher and the risk of infection was greater.

For practical purposes, all the sections were of the classical variety. The incisions, therefore, were all in the upper segment, though they varied in position and direction. In a very comprehensive paper, admirably compiled, he analysed 97 cases of ruptured scar, mostly collected from the literature. The maternal mortality was 30% and the fœtal mortality 77%. From a study of the figures he came to the conclusion that the predisposing causes for rupture were:

(1) Implantation of the placenta on the scar, leading to hæmorrhage.

(2) Sepsis, which he considered as the most important single cause. He took as evidence of infection pyrexia following the Cæsarean section and thinning and fibrosis in the resultant scar. This is circumstantial evidence only, and pyrexia in the puerperium may be due to other causes than infection in the scar. Puerperal pyrexia was common even in those scars which did not rupture and, of all those that did, a quarter were apyrexial. Fibrosis and thinning of the scar may be only the result of trauma, hæmorrhage or faulty apposition.

(3) Suture material. This is probably of more importance in the classical than in the lower segment operation.

(4) Accidental factors, such as hydramnios, version, antepartum hæmorrhage, prolonged labour or the administration of pituitary extract.

He considered that the site of the scar in the upper segment, where muscular contractions were present and involution was progressing rapidly, had a deleterious effect on sound healing. He noted a varying interval between the subsequent rupture of the scar and the previous Cæsarean section from less than one year to as many as twelve, and in some cases there had been one or more intervening vaginal deliveries.

In order to assess the frequency of rupture he was able to collect 1,103 cases of Cæsarean section performed between 1912 and 1918 from some 25 sources, and followed up since then (Table I). Of these 487 subsequently became pregnant, with 78 vaginal deliveries, 47 abortions, 352 Cæsarean sections, 18 ruptured scars and 86 were still pregnant. (Some of the 487 had more than one pregnancy.) If we include the Cæsarean sections, vaginal deliveries and ruptured scars we have 448 patients with 18 ruptured scars, that is to say, 4%, a figure that has stood till now as the likely percentage of classical Cæsarean scars to rupture. However, some two-thirds of the ruptures occurred during labour or the last week or two of pregnancy, and the risk of labour is, therefore, 12 ruptured scars among 90 vaginal deliveries, so that the risk of ruptured classical scar during a subsequent labour is some 13% to 14%. With such a risk, and its attendant fœtal mortality, it is doubtful whether it is justifiable to allow a patient with a classical scar to have a subsequent vaginal delivery.

Many distinguished obstetricians joined in the discussion: Professor Munro Kerr, Mr. Barris, Mr. Leonard Phillips, Dr. Amand Routh, Dr. C. Oldfield, Dr. Herbert Spencer, Dr. Blair Bell, Dr. E. O. Croft, Mr. Furneaux Jordan, Dr. Fothergill, Dr. Gough, Dr. W. Fletcher Shaw, Dr. J. W. Bride, Mr. Clifford White and Dr. Lapthorn Smith.

They were all in general agreement with the opinions expressed by Sir Eardley Holland. Professor Munro Kerr suggested that an incision in the lower segment would leave a sounder cicatrix because of the lessened muscular activity and rapidity of involution. He described his method of lower segment section and said he had performed the operation eighteen times. To-day the lower segment operation is almost entirely employed by skilled obstetricians, to the exclusion of incisions in the upper segment.

TABLE I (Holland, 1920)

| | |
|---|---|
| Total number of Cæsarean section patients (exciuding fatal and sterilized cases, and cases of repeated Cæsarean section where the first operation was performed prior to 1912) | 1,60 |
| Number followed up .. .. .. .. .. .. .. .. .. | 1,16 |
| Number in whom no subsequent pregnancy occurred .. .. .. .. .. | 61 |
| Number who subsequently became pregnant .. .. .. .. .. .. | 48 |
| Results of pregnancies: | |
| Delivery by natural passages .. .. .. .. .. .. .. .. | 78 |
| Repeated Cæsarean section .. .. .. .. .. .. .. .. | 352 |
| Abortion .. .. .. .. .. .. .. .. .. .. .. | 47 |
| Pregnant now .. .. .. .. .. .. .. .. .. .. | 86 |
| Rupture of scar .. .. .. .. .. .. .. .. .. .. | 18 |

In 1949 Mr. McIntosh Marshall analysed some 7,762 Cæsarean sections from 19 hospitals, performed between the years 1943 and 1947 from among 125,179 deliveries. During this time 29 cases of ruptured uterus came under treatment, 10 of these being ruptured scars (9 classical and 1 lower segment Cæsarean section). There were no maternal deaths amongst the ruptured scars. The fœtal mortality was not given. We do not know the number of vaginal deliveries taking place at these hospitals over this period among mothers with a Cæsarean section scar in the uterus. As there were rather less than a quarter classical among the Cæsarean sections we may assume that the lower segment scar is less likely to rupture. Furthermore, the lower segment scar, should it give way, is less likely to rupture before labour begins.

The signs of ruptured scar may be confusing. The classical signs of rupture, cessation of uterine contractions, recession of presenting part, vaginal bleeding, severe lower abdominal pain, the absence of the fœtal heart sounds and collapse of the patient are often absent. Pain may be minimal and contractions may continue. An apparent bulging of the scar during a uterine contraction probably indicates that the uterus has already ruptured, and no time should be lost in performing a laparotomy. It is said that hæmorrhage is less from a ruptured scar than from a spontaneous rupture of uterus, but this has not been my experience with classical section scars. The mortality is lower when the scar ruptures than in a case of rupture due to other causes. This is probably because a close watch is kept during labour on a patient with a scar in the uterus, so that little time is lost between the rupture and the performance of a laparotomy.

Though infection of the wound may play some part in predisposing to a rupture I do not believe it is nearly so important as careful repair of the uterine wound at the time of the Cæsarean section. Accurate approximation of the wound edges may be difficult to accomplish because after delivery the retraction of the upper segment leaves the upper edge shorter than the lower one. This difficulty can be overcome by placing the third suture (after one at each angle) in the mid-line. Otherwise, looping of the lower edge may occur at the corner of the incision. It is best not to apply pressure forceps of any kind to control hæmorrhage from the uterine wall as they must leave some muscle damage and scar tissue in their wake. I do not know whether the present fashion of tearing instead of cutting the lower segment incision will lead to an increased number of ruptures. The widening use of Cæsarean section in recent years has increased the number of sections performed for non-recurring indications, and a large number of mothers having had a Cæsarean section may be expected to undergo a future vaginal delivery.

In the past fifteen years 6 ruptured scars only have been dealt with at the West Middlesex Hospital, 5 classical and 1 lower segment Cæsarean section, which seems the usual proportion. I am happy to say that none of these Cæsarean sections was performed at the West Middlesex Hospital, although one ruptured scar from our own series of 1,066 sections occurred during that time. She was admitted to another hospital for her second labour. Unfortunately, we have only listed labours following Cæsarean section in the disease index since 1949 and, during the last four years, 31 cases only have been so delivered. 26 of these had had a lower segment operation and 5 a classical. Over this period only 1 patient with a ruptured scar was admitted. Her first baby was delivered by lower segment Cæsarean section in 1949 in Lincolnshire, the indication being incomplete breech. She had a spontaneous delivery in 1950 at the West Middlesex Hospital and she ruptured her scar at the onset of her third labour. These figures are, of course, too small to give any indication of the incidence of ruptured lower segment, but the frequency seems to be of the order of 1% or less, provided the Cæsarean section was performed in a maternity unit with a good standard of efficiency.

On the whole, it seems reasonable to say that after a classical Cæsarean section no patient should be allowed a vaginal delivery whereas, following lower segment operation, vaginal delivery may take place provided:

(1) There are no obstetrical contra-indications.

(2) That the delivery takes place in hospital.

(3) A careful watch is kept on the scar.

External version and intra-uterine manipulations are best avoided in these cases.

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**Dr. R. M. Corbet:** I have seen 38 cases of rupture of the pregnant uterus, 10 of which terminated fatally, a mortality of approximately 26% (Table I). The mortality rate, however, dropped sharply once it was recognized that the approach should be through the abdomen, when it was even suspected that rupture had occurred, and not through the vagina. Since 1928 only 3 patients have been lost, 1 from peritonitis (1929), 1 from hæmorrhage undiagnosed (1937), and 1 from mesenteric thrombosis (1942).

TABLE I.—RUPTURED UTERUS 1923–1953

| | Cases | Mortality |
|---|---|---|
| 1923–1928 .. .. | 12 | 7 |
| 1929–1953 .. .. | 26 | 3 |
| Total | 38 | 10 |

| *Situation of rupture* | Cases |
|---|---|
| Upper segment .. .. .. .. | 9 |
| Lower segment .. .. .. .. | 8 |
| Both segments<br>Lateral wall tears } .. .. .. | 21 |

| *Position of rupture in the 10 fatal cases* | Cases |
|---|---|
| Upper segment—anterior wall .. .. | 1 |
| Lower segment—posterior wall .. | 2 |
| Both segments—lateral wall .. .. | 7 |

| *Scar ruptures* | Cases |
|---|---|
| Upper segment Cæsarean .. .. | 6 |
| Lower segment Cæsarean .. .. | 3 |
| Previous perforation .. .. .. | 1 |
| Myomectomy .. .. .. .. | 1 |

Since laparotomy, followed by hysterectomy or repair, has become the main line of treatment, the classification of rupture into complete or incomplete has lost its importance. The situation of the rupture, however, is of significance. In more than half of these cases (21) the tear involved the lateral wall and extended into both upper and lower segments. 8 of the 9 upper segment ruptures and 3 of the 8 lower segment ruptures occurred through previous scars.

Vant of Edmonton has pointed out the danger of the lateral wall tear. This series supports his view. In the 10 fatal cases the rupture occurred in the lateral wall seven times, in the posterior wall lower segment twice and the anterior wall upper segment once. 6 of the lateral wall ruptures and the anterior wall rupture died of hæmorrhage.

*Rupture of scars.*—Undoubtedly the scar of an upper segment section is much more likely to rupture during pregnancy than the scar of a lower segment section; indeed, this latter condition has seldom been recorded. When labour is established I believe that there is little difference in the chance of rupture of either scars. In only 1 of the 6 upper segment scar ruptures was the patient definitely in labour. In the 3 lower segment ruptures the patients had been in labour for some hours in an attempt to deliver vaginally. So far I have not had a rupture of an upper segment scar where the patient had been allowed to attempt a vaginal delivery.

*Difficulties of diagnosis.*—These occur chiefly in the spontaneous ruptures; the classical signs may be entirely lacking. The pains may not cease, indeed, I believe commonly do not cease until the

uterus has emptied itself into the peritoneal cavity or vaginally. 2 of these fatal cases delivered spontaneously. The presenting part will not recede if the greatest diameter is through the pelvic brim. There may be no vaginal hæmorrhage until the baby is born or the presenting part disturbed in attempts at delivery. The patient may show little signs of shock although the uterus is obviously ruptured, or profound shock with no other signs of rupture. In most spontaneous ruptures there is no stage of threatened rupture. The way to avoid mortality is to keep the condition in mind and to act on suspicion rather than certainty.

**Professor W. C. W. Nixon:** *Spontaneous Vaginal Delivery after Rupture of Uterus in a Previous Pregnancy*

CASE REPORT

Mrs. L. B., aged 29.

This patient had a normal delivery on 3.7.50 of an 8 lb. 4 oz. (3,700 grammes) baby after a labour of fourteen and three-quarter hours.

*Previous obstetric history.*—24.3.47: Abdominal hysterotomy at another hospital for bleeding at 20 weeks. Patient unmarried. Operation report: "The placenta was on the anterior wall of the lower uterine segment with a placenta succenturiata directly over the cervix." The puerperium was complicated by a pulmonary infarct (pyrexia for three weeks).

12.6.48: Rupture of uterus at 36 weeks. Her pregnancy had been normal until the day before, when she complained of abdominal pain. She was admitted and the pain ceased until the next day, when she presented the picture of internal hæmorrhage.

At laparotomy the fœtus and placenta were lying free; there was much blood but the uterus was contracted and not bleeding. A rent extended from just above the internal os to 1 cm. over the fundus. The edges were pared and the uterus closed with two layers of catgut sutures (No. 1). The uterine muscle was particularly friable but the histology was normal—there was neither increase nor diminution of collagen and nothing to suggest fatty change. The puerperium was normal. First menstruation thirty-three days after operation followed by regular cycles.

3.7.50: Patient now married. Normal delivery. The present pregnancy was uncomplicated but the patient was brought into hospital for one month before her delivery. A placentography and pelvimetry were done, both of which were normal. Labour started spontaneously at term and ended normally (1st stage—13¼ hours; 2nd stage—75 minutes; 3rd stage—5 minutes).

*Conclusion.*—An abdominal hysterotomy at 20 weeks was the factor that predisposed to the rupture of the uterus in the second pregnancy. When the uterus is conserved after rupture there is no reason why the next delivery should not be normal. The case should be managed in the same way as one which has had a previous Cæsarean section.

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# Section of Pædiatrics

President—C. T. POTTER, M.D., F.R.C.P.

[*October* 23, 1953]

**Actinomycosis of the Chest Wall.**—N. J. ROTHFIELD, M.B., B.S.(Sydney), D.C.H. (for TREVOR P. MANN, M.D., M.R.C.P.).

*History.*—A boy aged 9 was admitted to the Royal Alexandra Children's Hospital, Brighton, on 22.6.53. He was in good health until one month before admission, when he first complained of a dry, irritating, unproductive cough, and shortness of breath. These symptoms became gradually worse, and loss of weight and increasing lassitude were observed. Five days before admission he complained of pain in a localized area on the back of the chest wall on the left side, and a tender swelling appeared there.

*Past history.*—Nothing significant apart from a slight blow on the left side of the chest several weeks before the onset of symptoms.

*On examination* there was a tender, rounded, non-fluctuant swelling, neither hot nor red, measuring approximately 3 in. × 3 in., centred over the eleventh left rib, and extending from the posterior axillary line to the scapular line. The respiratory excursion was diminished on the affected side, and there were dullness, diminished air entry and inconstant crepitations over the left lower lobe region. Dullness extended upwards approximately to the angle of the scapula, at which level there was localized bronchial breathing.

*Investigations.*—Blood count gave no significant information. Mantoux negative to 1/100 dilution. Intravenous pyelogram, X-ray of the spine and barium swallow showed no abnormality.

Chest X-rays: considering the extent of the physical signs, these showed surprisingly little. The outstanding features were:

(1) A triangular opacity behind the heart shadow, produced probably by consolidation in the posterior basic segment of the left lower lobe; though a localized effusion in the mediastinal reflection of the pleura was considered as an alternative.

(2) Pleural thickening on the left side.

(3) Ill-defined opacities of bronchopneumonic type in both the right and left lower zones.

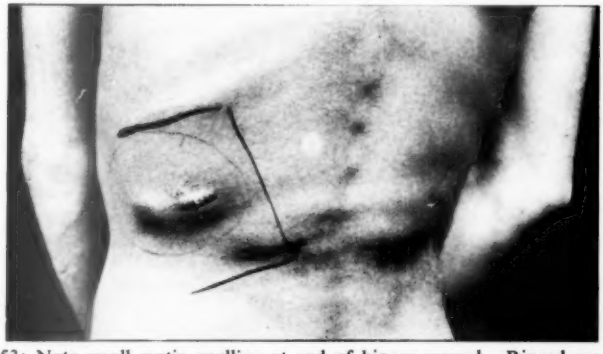

FIG. 1.—August 1953: Note small cystic swelling at end of biopsy wound. Ringed area indicates site of presenting tumour.

*Progress.*—While initial investigations proceeded, the child ran a low-grade fever rising in the evening to 100–101° F. Nine days after admission the swelling was examined under general anæsthesia and aspirated with a wide-bore needle; only a small amount of blood-stained fluid was withdrawn, showing relatively few polymorphs on microscopy, and sterile on culture. Taking into account the inconclusive investigations and exploratory findings, a tentative diagnosis of low-grade osteomyelitis of a rib was made, and penicillin commenced in dosage of 4,000,000 units daily by intramuscular injection; reduced after a week to 2,000,000 units daily. The temperature fell, apparently in consequence of treatment, and the lump lost much of its tenderness, though now redness and slight softening appeared in the centre.

FEB.

Three weeks after admission the possibility of actinomycosis was first considered, and this led to biopsy of the tumour a week later (20.7.53), which confirmed the diagnosis (sulphur granules in the fluid; *Actinomyces bovis* on culture).

Sulphamezathine in dosage of 2·0 grammes/day was now introduced, to supplement the penicillin; also potassium iodide in increasing doses. On 24.7.53 he looked ill; within three days the temperature had reached 104° F., by which time the appearance of a generalized erythematous rash suggested a diagnosis of drug intoxication. All medicaments were stopped, and within thirty-six hours the temperature was normal again.

Administration of streptomycin was commenced in dosage of 600 mg. b.d. Iodide was next reintroduced, without apparent ill-effect, and increased to a dose of 10 grains t.i.d.

On 6.8.53 a small lump appeared at one end of the biopsy wound, suggesting imminent breakdown (Fig. 1); this was averted, however, by 6 exposures to deep X-ray, given on alternate days.

At the time of presenting the case, three months' treatment with streptomycin was completed. Clinically, progress was satisfactory; he was up and about, afebrile, and gaining weight. A recent blood sedimentation rate was normal and a radiograph of the chest showed considerable improvement in the changes previously described. The original swelling had subsided, but there were two small fluctuant areas in the line of the biopsy incision.

POSTSCRIPT (November 1953).—The two fluctuant areas were incised and curetted; sulphur granules found. Streptomycin and potassium iodide are continuing. N. J. R.

**Generalized Lipodystrophy. Infectious Mononucleosis. Mild Infantile Hemiplegia.**—JOHN DAVIS, M.B. (for J. P. M. TIZARD, M.R.C.P.).

S. C., female, aged 31 months, the older child of young, healthy non-consanguineous parents, was born at full term after an uncomplicated pregnancy and labour, weighing 7 lb. 5 oz. She was healthy, and developed normally as an infant, but never exhibited a very good appetite. She was noticed to drag her right leg when she learned to walk: a symptom which her parents related to an immunizing injection given into the right thigh a month or so previously.

Her present symptoms appeared when she was 20 months old, after a severe but otherwise typical, attack of measles: while convalescent she lost all appetite, and several pounds in weight, and was found by her doctor to have visibly enlarged lymph glands in all major nodes. She had a second undiagnosed febrile illness of a week's duration during her mother's second confinement in January, and following this, wasted more rapidly and became very fractious and miserable. She was admitted to Paddington Green Children's Hospital in March 1953, and found to exhibit the abnormalities reported below. Diagnoses of lipodystrophy and infectious mononucleosis were made at that time. Since her discharge, she has gained several pounds in weight and grown rapidly taller, but her physiognomy has not altered and she has continued to run a low fever (100° F. P.R. nightly). She is said to drink and void excessive quantities of fluid, and continues to wet her bed almost every night. Her hair which had previously been quite straight, became curly in August.

*Physical examination.*—A tall, muscular-looking girl, with prominent veins and no appreciable subcutaneous fat anywhere. There is a suggestion of exophthalmos, and she is alert and nervous (Figs. 1 and 2).

T. 100° F. P. 120.

Height 3 ft. 2¾ in. Weight 2 st. 6 lb. 9 oz. (Ht. 90. Wt. 80—percentile).

C.V.S.: Moderate persistent tachycardia. R.S.: Trachea deviated to right. C.N.S.: Slight wasting of, and increase in tone and deep reflexes in the right leg as compared to the left.

Abdomen: Liver enlarged 1 fingerbreadth; spleen palpable.

E.N.T. healthy.

Skin: Folds of skin, pinched between finger and thumb equally meagre in all areas; face, trunk, arms, buttocks and legs all being affected (Fig. 2).

Glands: firm, discrete mobile, moderately enlarged glands palpable in occipital, cervical, axillary, epitrochlear, and inguinal nodes.

B.P. (after crying) 120/90.

*Biopsy of skin from buttocks.*—The dermis and epidermis appear normal. The only evidence of subcutaneous tissue is a small area in the H. and E. section consisting of sparse fat spaces embedded in connective tissue infiltrated with plasma cells, histiocytes, multinucleated cells and eosinophils—reminiscent of subcutaneous fat necrosis of the newborn.

*Blood picture.*—Hb 92% (13·7 grammes %); R.B.C. normal in appearance. Film not streaky. E.S.R. 3 mm. in the first hour. A number of atypical large mononuclears. Very suggestive of glandular fever. Total W.B.C. 14,000 per c.mm.:—neutrophils 5,000 (34%) no nuclear shift, eosinophils 1%, basophils 2%, lymphocytes 7,000 (50%), monocytes 3%, plasma cells 1%, atypical large mononuclears 1,300 (9%).

*Paul-Bunnell tests.*—18.3.53: Titre of unabsorbed serum: 1 in 56; titre of serum absorbed by ox cells: 1 in 56; titre of serum absorbed by guinea-pig kidney: 1 in 28. The titre, combined with the atypical absorption pattern, strongly supports the diagnosis of glandular fever.

FIG. 1.

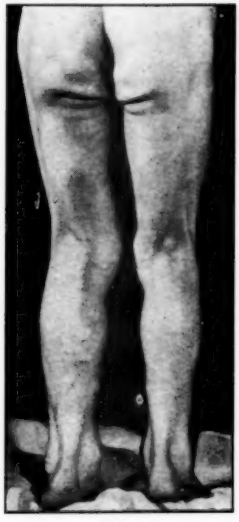

FIG. 2.

15.6.53: Titre of unabsorbed serum: 1 in 28; titre of serum absorbed by ox cells: 1 in 14; titre of serum absorbed by guinea-pig kidney: 1 in 14.

*Liver function tests.*—18.3.53: Blood urea: 35 mg.%. Thymol turbidity (MacLagen): 13 units (considerable increase). Serum colloidal gold (MacLagen) partial precipitation (4).

15.6.53: Serum thymol turbidity: 34 units. Serum colloidal gold: slight precipitation (2). Serum cholesterol: 250 mg.%.

Cholesterol.—250 mg.% (slight increase).

*Urine.*—Twenty-four-hour intake 16; output 15 oz. Sp. gr. 1020. No sugar or other abnormal constituents.

*Blood sugar curve.*—Fasting level 68 mg.%; level at ½ hour 138; level at 1 hour 136; level at 1½ hours 76; level at 2 hours 68.

Dose of glucose 17·5 g. All specimens of blood were lipæmic.

X-rays: Chest—trachea deviated to the right. Bones and skull normal; bone age 4½ years.

There are only 4 previously reported cases of generalized lipodystrophy in children (Feer, 1915; Weber and Gunewardene, 1919; Hansen and McQuarrie, 1940; Corner, 1952). This case is of interest because of the association of abnormally rapid growth with disappearance of the subcutaneous fat depots. The term lipodystrophy is used advisedly: the fact that the child has no muscle wasting, and is a normal weight for her over-average height, the failure to demonstrate the presence of any subcutaneous fat in a satisfactory biopsy specimen, and the absence of facial subcutaneous fat, which persists in wasting diseases, making it very unlikely that the condition is due to inanition; but it is employed descriptively rather than as the name of a disease entity.

*Comment.*—It was suggested during the discussion that the patient might belong to the group described by Dr. Alexander Russell (1951) at the British Pædiatric Association meeting in April 1951 under the title of the diencephalic syndrome. Dr. Russell's cases had features (generalized wasting, advanced bone age, and temporary acceleration of growth) in common with the child described here, but also others (tendency to hypoglycæmia, peculiar temperament, low blood pressure, diabetes insipidus, signs of intracranial tumour) which she lacks. There is no evidence which makes it possible either to confirm or to deny the suggestion. Dr. Russell, who has now seen the child, thinks it likely that she has a diencephalic lesion, probably a glioma—and she will be followed with that possibility in view, but full air studies have failed to reveal such a lesion.

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**Multiple Non-tuberculous Pulmonary Calcifications. ? Phleboliths.**—JOHN LORBER, M.D., M.R.C.P.

P. H., born 5.3.42. Female. Present age 11 years 7 months.

This child had symptoms of bronchial asthma from the age of 1 year. She has a family history of asthma. She was admitted to hospital on 6.3.47, at the age of 5 years, with severe acute pulmonary infection with high fever. On admission she had clinical and radiological evidence of consolidation of the right lower lobe (Fig. 1). There was some polymorph leucocytosis (12,500 white cells, 72% polymorphs). Mantoux 1/1,000 negative. She was treated with Sulphamezathine for nine days. High fever up to 104° F. persisted for six days, and because of that and because of the increasing X-ray changes she was given crystalline penicillin from 12.3.47 for six days. The temperature immediately returned to normal and remained so till discharge. There was, however, no corresponding radiological improvement for a long time and almost total collapse of the right lung developed, which was maximal sixteen days after admission (Fig. 2). The right lung gradually re-expanded. Bronchoscopy on 21.4.47 disclosed œdema and reddening of the mucosa of the right lower lobe bronchus, but no pus was present nor was any obstruction seen. The chest X-ray became normal at the beginning of May 1947, and she was discharged home.

FIG. 1.—Consolidation of right lower lobe.

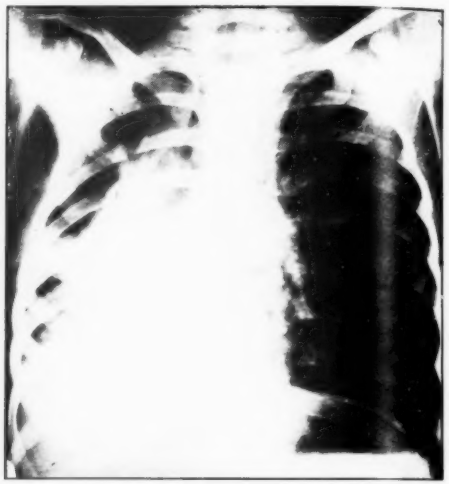

FIG. 2.—Almost total collapse of right lung with herniation of left lung across the mid-line.

FIG. 3.—Close-up view of right lung showing multiple diffuse round calcified shadows five years after acute illness.

She remained well during the next three years but subsequently reattended hospital because of recurrence of asthma and at that stage multiple calcifying opacities were found on X-ray in the right lung.

In October 1952 she was readmitted for investigations after an acute asthmatic episode. An unexpected physical sign was an oval-shaped patch of old choroiditis in the left fundus at 5 o'clock, which was of unknown ætiology. Skin tests were negative for tuberculin (Mantoux 1/100) histo-

plasmin, coccidioidin and toxoplasmin. Serological tests for toxoplasmosis were negative. A radiograph of the skull was normal, but in the radiograph of the chest disseminated, homogeneous round calcified foci were seen in the right lung which have not altered since (Fig. 3). In view of the past history and the apparent exclusion of the more recognized causes of pulmonary calcifications, these shadows are presumed to be phleboliths.

**Diphtheroid Meningitis Complicated by Hydrocephalus.**—M. C. JOSEPH, M.R.C.P., and C. T. POTTER, M.D., F.R.C.P.

R. O. Age on admission (3.8.53) 11 days. Birth weight 7 lb. 12 oz. Normal at birth.

Normal pregnancy except some excess vomiting. Normal delivery.

Mother's general health poor. Has mastitis with every birth. Had diphtheria at age of 10 years and was in hospital three months as a nasal carrier.

Baby was well until ninth day when there was a mucopurulent discharge left eye—treated with penicillin drops. 11th day (3.8.53) infant restless and at midday began having convulsions which continued on and off until admission to the Evelina Hospital.

*On examination.*—Fever 101·6° F. Poor cry. No meningeal signs. Pain on flexion both hips. Fontanelle tension normal. Head circumference 14½ in. Moro and grasp reflexes present. Heart-rate 140/150 per minute. Other systems normal.

*Investigations.*—13.8.53. *C.S.F.*: W.B.C. 3,900, polymorphs 84%, protein 110 mg.%. *Culture*: Pure growth of a diphtheroid.

13.8.53. *Blood culture*: Pure growth of a diphtheroid.

14.8.53: *C.S.F.*: W.B.C. 1,000, protein 360 mg.%. *Culture*: Pure growth of a diphtheroid.

14.8.53. *Blood count*: W.B.C. 18,000, polymorphs 11,000.

16.8.53. *C.S.F.* (ventricular puncture): W.B.C. 600, lymphocytes 94%. Sugar 50 mg%. *Culture*: Pure growth of a diphtheroid.

24.8.53. *C.S.F.*: W.B.C. 100, lymphocytes 88%, protein 264 mg%. *Culture:* sterile.

*Culture of C.S.F. and blood culture.*—An organism of the diphtheroid group was isolated after further incubation from the cultures from the lumbar C.S.F. It is identical with an organism cultured from the ventricular C.S.F. and with one from the blood culture, and no point of difference has been found. The organism from all sources is sensitive to penicillin, streptomycin, Aureomycin and chloramphenicol. No diphtheroid organisms were isolated from swabs taken from the infant's ear, eye or skin, but the vaginal swab grew a diphtheroid which, however, differed from that isolated from the C.S.F. and blood. Her mother, father and the midwife also had nose and throat swabs taken and additionally a vaginal swab from the mother; in none of these was a diphtheroid isolated.

*Progress.*—In view of the uncertainty of the organism causing the meningitis she was treated with intrathecal streptomycin, oral Aureomycin and systemic streptomycin for four days. The convulsions were controlled partially by chloral, and she was tube fed for the first few days. Her last fit was on the sixth day of her illness and on this day she began to take feeds from the bottle. She gained weight well and her skull circumference on discharge on the fourteenth day of her illness was unchanged. She was then seen weekly and four weeks later suddenly developed acute hydrocephalus, the skull circumference measuring 17½ in. and the anterior fontanelle over 3 in. wide and bulging. Air studies at the Guy's-Maudsley Neurosurgical Unit (Dr. B. H. Dawson and Dr. R. D. Hoare) revealed a block in the aqueduct of Sylvius, and Mr. Murray Falconer performed a Torkildsen's ventriculocisternostomy. Following operation she has remained well and the fontanelle has become slack and the head circumference decreased to 16½ in. She does not, however, follow light and her discs show some atrophy.

*Comment.*—Two cases of diphtheroid meningitis have been previously reported, one by Gibson (1935) and the other by Clapper and Carlquist (1945), but neither of these was in a newborn infant. Gibson reported autopsy findings and subsequent investigations of a meningitis due to a diphtheroid which was identical to our case. The patient was a man aged 40 years who died on the fifth day of illness. After death the C.S.F. contained 300 cells of which 70% were mononuclears; it is of interest that in the present case the C.S.F. on the fourth day was mainly mononuclear. Gibson injected the organism by various routes into guinea-pigs, rats, mice and rabbits and although death occurred in all the animals, the meninges were spread. Clapper's case was that of a 7-year-old child who died after six months' observation from meningitis and cerebral abscess. The organism was similar to *C. ulcerogenes* except that it differed from the latter in not fermenting sucrose. Experimentally, the organism had very low pathogenicity. Further studies on the pathogenicity of the diphtheroid in the present case are being studied (Shaw and Turk), but up to the present only local lesions have been produced and the animals still survive.

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**Diabetes Mellitus In An Infant Aged 39 Days.**—B. GANS, M.D., M.R.C.P.

First-born male infant of healthy parents, whose blood sugar curves are normal. Family history of diabetes in a paternal uncle.

The child weighed 5½ lb. at birth, was breast fed and was reported as always being hungry. He made good progress until two days before admission, when he refused his feeds and became irritable. He vomited once or twice, but his bowels remained normal.

On the day of admission he was 39 days old. He was semi-conscious, grossly dehydrated, and cyanosed. His respiratory rate was 85, temperature 99·6° F., rales were audible in both lung fields, and his white count was 17,600 with 74% polymorphs. A chest X-ray was within normal limits. A diagnosis of bronchopneumonia was made, this being the typical diagnostic pitfall in diabetic infants (Newcomb and Farrell, 1951). The baby was placed in an oxygen box, given an antibiotic, and a subcutaneous ("Hyalase") drip of Hartmann's solution was started. Next day his hydration was satisfactory, but he appeared even more desperately ill. The drip was discontinued, and four hours later he was again severely dehydrated. This rapid dehydration, and a strong smell of acetone in the baby's breath, led to a blood-sugar estimation. The result was 1,376 mg.%. His urine completely reduced Benedict's solution, and gave a strongly positive Rothera and ferric chloride test. The blood sugar is the highest recorded in an infant of this age, and the ketonuria is most unusual as most diabetic infants do not pass acetone in their urine even with high blood-sugar levels (Wylie, 1953).

*Course.*—The subcutaneous infusion of 1/2 N Hartmann's solution was re-started, and the baby received 50 units of soluble insulin hourly until the Rothera test was negative. Four hours later, when he had received 200 units, his blood sugar was 550 mg.% and his ketonuria had ceased. Next morning the blood sugar had risen to 745 mg.%, and ketones were again present in the urine. A further 50 units were injected, and the next blood-sugar estimation showed a level of 63 mg.%. The baby therefore received 250 units of insulin in twenty-four hours.

During the rapid descent of the blood sugar the baby became anuric for sixteen hours, and had innumerable convulsions. These appeared not to be due to hypoglycæmia as he did not sweat and blood-sugar values of 1,180, 825 and 550 mg.% were obtained whilst he was convulsing. Presumably the fits were due either to relative hypoglycæmia or to the effect of rapid osmotic pressure changes on the brain.

Hydration was maintained, first by 1/2 N Hartmann's solution without glucose. Later, when acetonuria had ceased, 5% glucose was added to the subcutaneous drip. After forty-eight hours an indwelling gastric drip of equal quantities of Darrow's solution and expressed breast milk was started. On the fourth hospital day the baby was able to take from the bottle. By this time his mother had lost her milk.

*Insulin requirements.*—After the first twenty-four hours five units of soluble insulin were injected before each four-hourly feed. In spite of hourly urine testing and twice daily blood-sugar estimations, perfect biochemical control proved impossible, but the baby appeared very well, and took his feeds avidly, even with blood-sugar levels of 400 mg.%. His respiratory rate was found to be an excellent guide to his progress, a rise heralding an increase in the blood-sugar level. No episodes of hypoglycæmia occurred after the first twenty-four hours. His insulin requirements have slowly decreased and are now 26 units per day. After six weeks of four-hourly injections of soluble insulin a change was made to one daily injection of 26 units insulin zinc suspension (Lente). A single daily injection proved unsatisfactory, but the baby is now well controlled on two daily injections of 13 units of this long-acting insulin.

*Diet.*—As soon as he was able to feed from the bottle the infant was allowed as much full-cream National Dried Milk as he would take. On the fourth hospital day he took 3 oz. four-hourly, and on the twelfth day 6½ oz. four-hourly. To enable him to lay down a reserve of glycogen 1 drachm of sugar was added to each ounce of milk. The quantity of sugar was slowly decreased to one drachm to each 4 oz. of milk in the next three weeks. During the first six weeks of his illness he gained an average of 14 oz. per week. Mixed feeds were introduced when he was 11 weeks old. He is now 15 weeks old and weighs 14 lb. 13 oz. There is no evidence of cataract, hypertension or retinal arteriosclerosis, but he has a well-marked subcutaneous fat atrophy of his right thigh. This first appeared after four weeks of treatment, an uncommonly early onset as it does not usually occur until some six months after the start of injections (White, 1946).

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# Section of Orthopædics

President—H. L-C. Wood, M.S., F.R.C.S.

[*November* 3, 1953]

## Observations on Cystic Tuberculosis of Bone, with a Report on Two Cases

By R. O. Murray, M.B., D.M.R.

*Radiologist, Lord Mayor Treloar Orthopædic Hospital, Alton, Hants.*

Infection of the skeletal system by the tubercle bacillus usually involves joints. The joint may be the site of a primary infection or may become secondarily involved by the spread of an endosteal focus. This is particularly seen in the spine and, in children, by spread from metaphyseal foci in the long bones to which the epiphyseal plate proves no barrier. It is the purpose of this paper to review briefly the types of pure infection of bone which may occur and to discuss in some detail a rare form of the disease which has been described as multiple pseudocystic tuberculosis of bone (Komins, 1952).

Pure infection of bone by the tubercle bacillus is rarer than the involvement of joints. Such infections, provided that the articular surfaces and the synovial membranes are spared, tend to follow a benign course. The great majority of cases occur in undernourished children and show only solitary lesions. The long bones are most commonly affected, but involvement of the short bones and of the flat bones is equally well recognized. Disseminated lesions do occur but they tend to remain confined to one of these types of bone. In such instances the terminology suggested by Alexander and Mansuy (1950) of "Disseminated Bone Tuberculosis" seems applicable.

In the *long bones*, as indicated before, the metaphysis is the usual site of infection but diaphyseal lesions are also found, which may prove difficult to differentiate from a pyogenic osteomyelitis.

In the *short bones* the most common form of infection is tuberculous dactylitis or spina ventosa in which the whole medulla is involved. In these cases the inner aspect of the cortex is eroded and subperiosteal new bone is laid down so that the affected short bone has the classical appearance of being inflated with air. Multiple lesions in the bones of the hands and the feet are common in such cases, but examination of serial radiographs shows that they tend to be consecutive rather than simultaneous in onset; affection of the joints is unusual.

In the *flat bones*, apart from the spine, which is the commonest of all lesions, the pelvis is the most frequent site of attack with a focus similar in appearance to that seen in the long bones and from which spread to a joint may take place. The skull may be the seat of osteolytic foci, which are commonly multiple.

Before proceeding to describe cystic tuberculosis of bone, reference should be made to the fact that confusion has arisen in the past by description under that title of conditions which should be recognized by other names. Komins (1952) has attempted to clear up the confusion in the early literature between the lesions in cases of this type and those of sarcoidosis. This confusion appears to have been accentuated by the description of Jüngling (1920) of the lesions found in the small bones of the hands and feet in sarcoidosis. To this condition he gave the title of "Osteitis Tuberculosa Multiplex Cystica"; the last word was subsequently altered, to indicate its pseudocystic nature, to "Cystoides". Komins suggested that it should be called "Osteitis Multiplex Cystoides Sarcoidosa".

Solitary diaphyseal foci in long bones (Vangorder, 1934), and tuberculous dactylitis have also been described as cystic tuberculosis.

That the confusion persists, however, is shown by a recent account of unusual tuberculous changes in the short bones of the hand and foot, with other lesions resembling sarcoidosis, under the title "Multiple Cystic Tuberculosis of Bone (Jüngling's Disease)", (Girdwood, 1953). It is held by many authorities that the term "Jüngling's disease" should be reserved for the osseous manifestations of sarcoidosis.

The conditions which should be differentiated are therefore:

(1) *Metaphyseal endosteal focus*—traversing epiphyseal plate.

(2) *Tuberculous dactylitis*—consecutive lesions confined to short bones—often allied with cystic tubercle (Connolly, 1938).

(3) *Diaphyseal tuberculous osteitis*—solitary and caseating—this is a much more chronic lesion.

(4) *Sarcoidosis*—The appearance is typical and is never accompanied by abscess formation. Granulomatous deposits are associated with skin, gland and lung lesions.

*Cystic tuberculosis*, however, manifests itself differently. Not only is the individual lesion easily distinguished from the foregoing, but it follows a different course.

The disease is rare. Komins accepted 31 cases from the English literature and reported 3 more. Only 1 of these (Connolly) has been recorded in this country, most of the cases reported occurring in coloured races in tropical and semitropical regions, usually affecting young and undernourished children. During the last seven years the writer has seen over 1,000 cases of bone and joint tuberculosis. Among this number the first case here described was encountered; the other was found during a review of old cases and has not been seen personally.

Failure to overcome a primary, and usually pulmonary, infection is followed by a spread through the blood stream to other parts of the body, and by the formation of multiple abscesses. With these are associated areas of medullary bone destruction which have some uniformity of pattern.

The following features are characteristic:

(1) The lesions tend to be simultaneous in onset and to progress and regress in harmony. They have a predilection for the long bones, particularly the tibiæ, but concomitant involvement of the short bones and the flat bones is also found.

(2) The areas of destruction tend to be oval in the long axis of the bone, with regular, clearly defined margins, in which no early bone reaction is observed. The lesions are thus pseudocystic in appearance.

(3) Fusiform expansion of the bone may occur later and is likely to be associated with an overlying lamellar periostitis. These features were not present in the adult case now reported.

(4) The epiphysis usually, but not invariably, offers a barrier to the spread of infection, unlike the more common solitary metaphyseal focus.

(5) Joint involvement is, therefore, uncommon but, when it does take place, mobility is not permanently impaired.

(6) Erosion of the cortex is almost invariable. This leads to the formation of abscesses which often break down to form discharging sinuses. Sequestrum formation, however, is extremely rare.

## Case Reports

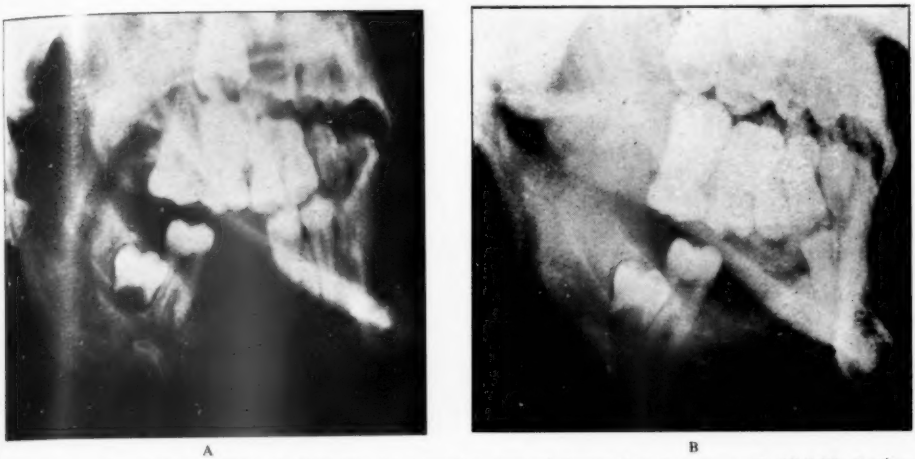
*Case I.*—A female office worker, aged 18, was admitted to Morland Clinics on 24.6.49 complaining of multiple soft-tissue swellings which had developed during the previous nine months. Some of these had broken down with resultant discharging sinuses. One year previously she had had pulmonary tuberculosis in which activity had subsided after three months.

A B

Fig. 1 (*Case I*).—*Left hand.* A, 27.6.49: Cystic destruction of fourth terminal phalanx with erosion of the cortex on the radial side. Subarticular decalcification of interphalangeal joints of fourth and fifth fingers. B, 13.7.50: Lesion healed.

A B

Fig. 2 (*Case I*).—*Right hand.* A, 27.6.49: Large circular area of destruction in base of fifth proximal phalanx, with apparent involvement of articular surface. Subarticular decalcification of interphalangeal joints of fourth and fifth fingers. B, 13.7.50: Lesion healed. Joint surface irregular.



A B

FIG. 3 (*Case I*).—*Left mandible.* A, 3.10.49: An extensive area of destruction is shown. B, 12.6.50: Lesion healed. A premolar has been removed.

A I A II B

FIG. 4 (*Case I*).—*Right knee.* A, 3.10.49: Typical cystic area of destruction, with slight surrounding sclerosis in upper part of tibia. The head of the fibula has been destroyed with involvement of the proximal tibio-fibular joint. B, 13.7.50: Lesion healed without more than a trace in the tibia. Head of the fibula recalcified but irregular.

Discharging sinuses were present over the right elbow, right fifth finger, left fourth finger, the inner aspect of the left heel, the head of the left fibula and the left mandible. The last discharged unpleasantly into her mouth. Palpable swellings were also found over the right upper calf and the left internal malleolus. Limitation of flexion of the right knee was considered to be associated with the abscess in the right calf rather than with joint involvement. The blood count was normal. E.S.R. in one hour was 56 mm.

The patient was treated by:

(1) Recumbency, with immobilization of the wrists and the affected finger and of the lower limbs.
(2) Ext. PAS therapy (20 grammes daily, six days a week, for sixteen months).
(3) Aspiration of the abscess in the right calf.

A B

FIG. 5 (*Case I*).—*Left knee.* A, 3.10.49: Tibia shows a comparable and symmetrical lesion (*cf.* right knee). B, 13.7.50: Lesion has healed almost without trace.

Subsequently an abscess appeared over the right hip. Pus from both abscesses gave positive animal inoculation tests for tubercle bacilli. The histological findings from a biopsy of the gum over the left mandible were suggestive of tuberculous infection.

The radiological lesions in the fingers, left mandible and knees are illustrated in their active and healed phases (Figs. 1, 2, 3, 4 and 5). Similar but less marked lesions were observed in the right external humeral epicondyle and left calcaneum.

All the lesions healed satisfactorily and the patient became ambulant on 1.2.51 and was discharged on 27.4.51. On 24.10.53 she was entirely well with no residual disability. The right fifth metacarpophalangeal joint was fully mobile.

*Comment.*—The areas of bone destruction were found to underlie all the soft-tissue swellings, with the exception of that over the right hip, where osteoporosis alone was demonstrated. Thus all types of bone were affected. In general the lesions were circular or oval, with little or no evidence of reactionary sclerosis. In some cases the cortex was eroded, but the only joints involved were the right fifth metacarpophalangeal and the right proximal tibio-fibular. No periostitis and no sequestra were seen. Examination of the remainder of the skeleton was negative. Radiological review of all the lesions on 24.10.53 showed no significant change.

*Case II.*—A female child, aged 4, was admitted to the Norfolk and Norwich Hospital on 5.6.42, with multiple swellings of one year's duration, affecting both wrists and the dorsum of one foot. Aspiration of the last yielded pus which gave a positive animal inoculation test for tubercle bacilli. The patient was transferred to the Treloar Hospital, Alton, on 21.6.42, when examination revealed the presence of further swellings on the dorsum of the other foot, the left elbow, the right arm and over the right malar region. These subsequently broke down to form pus-discharging sinuses. Animal inoculation again showed the condition to be tuberculous. The Pirquet and Mantoux tests were positive. The Wassermann reaction was negative.

Treatment by conservative measures and light therapy caused the activity of the condition to subside apd the sinuses to heal. The patient was discharged well and with no residual disability on 13.9.44, since when no follow-up has been possible.

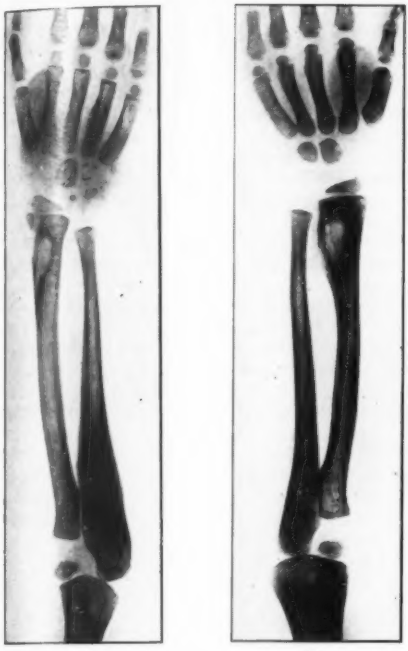
### *Radiological Appearances*

(Case II)

18.5.43: *Left arm* (Fig. 6A). An area of destruction is evident in the distal end of the radius; the cortex has been eroded and the infection has not respected the epiphysis. Some sclerotic reaction is evident. The hamate bone in the carpus has undergone almost complete destruction, being only represented by a ring of fragments. The shafts of the second, third and fourth metacarpals show obvious periostitis. Bilateral destructive changes comparable to tuberculous dactylitis are seen in the first metacarpals. A central area of destruction with considerable reactionary sclerosis around it is also evident in the proximal end of the ulna. This has caused fusiform expansion of the bone with an overlying lamellar periostitis.

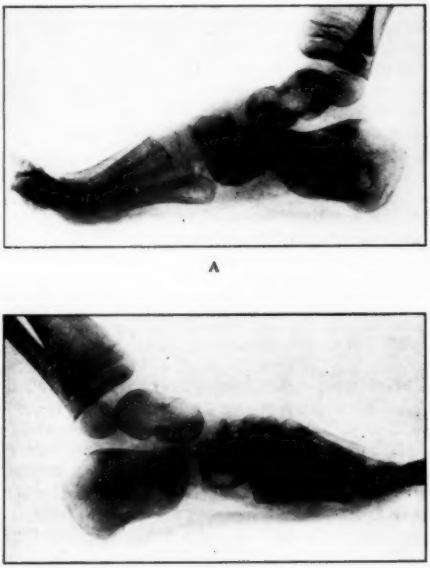
18.5.43: *Right arm* (Fig. 6B). A similar area of destruction is seen in the distal portion of the radial shaft. Fusiform expansion has occurred, with some surrounding sclerosis and a little periostitis. Some cortical erosion is present. A similar lesion is present in the lower end of the humerus, with some overlying periostitis.

18.5.43: *Right foot* (Fig. 7A). A circular area of destruction is seen in the cuboid. On the inferior aspect the cortex has been eroded. Early reactionary sclerosis is evident around this lesion. Irregular and less definite destruction is present in the calcaneum



A B

FIG. 6 (*Case II*).—18.5.43:
A, left arm. B, right arm.

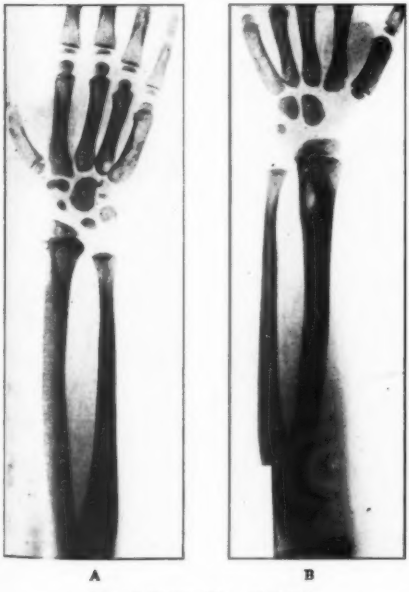


A



B

FIG. 7 (*Case II*).—18.5.43:
A, right foot. B, left foot.



A B

FIG. 8 (*Case II*).—31.5.44:
A, left arm. B, right arm.

A

B

FIG. 9 (*Case II*).—31.5.44:
A, right foot. B, left foot.

18.5.43: *Left foot* (Fig. 7B). An oval area of osteoporosis, rather poorly defined, but with a slightly sclerosed margin is present in the cuboid. In the body of the calcaneum a larger and more obvious lesion of a similar type is present.

Radiographs taken thirteen months after the original investigation (Figs. 8 and 9), show all the lesions to have improved. The periostitis has universally regressed. The left hamate is still fragmented but the advanced carpal ossification present suggests this area has been hyperæmic. The radial lesions are well sclerosed and have almost resumed their normal contour. The left ulnar lesion has resolved in a similar fashion. Unfortunately no film of the humerus is available.

The lesions in the left cuboid and calcaneum are only represented by a little residual sclerosis, but that in the right cuboid is still clearly defined as a circular translucency surrounded by well-marked sclerosis.

Thus multiple areas of bone destruction were again found to underlie the abscesses. Once more they are seen to be oval or circular, to erode the cortex and to affect the long and short bones. (Although no adequate radiograph is available it seems likely that the maxilla was also involved.)

In this case, however, other features are evident.

(1) Some of the lesions have caused fusiform expansion of the long bones. This may be due to the fact that the disease has affected young and growing bone.

(2) Considerable periostitis of a lamellar type is observed. The last affected some of the metacarpals and, it should be reported, a slight reaction could be seen on the upper ends of both tibiæ, of which the medulla appeared to be rarefied, though no definite area of destruction was shown. This seems comparable to the osteoporosis of the right acetabulum in Case I, in which an abscess formed with no definite underlying bone lesion.

(3) Some of the lesions show a dense sclerotic reaction, to such a degree, indeed, that permanent bone stigmata remained after the infection had subsided. It is tempting to regard this as a result of secondary pyogenic infection, but the change was apparently present before the sinuses formed. This appearance corresponds to the findings in other juvenile cases. It may be associated with activity of the disease for a longer period than the history records.

(4) The infection did spread across the lower radial epiphyseal plate, but there is no history of subsequent joint involvement.

## Discussion

Consideration of these cases allows certain new conclusions to be drawn.

Case I shows that the condition can occur in an adult, with widespread dissemination of the infection. In this case no fusiform expansion of the bones occurred and the customary periostitis was absent. These findings may well be associated with the fact that growth had ceased. The only joints involved were the right fifth metacarpophalangeal and the right proximal tibio-fibular. Two cases in adults, showing a certain similarity, but with a smaller number of foci, were reported by Van Alstyne and Gowen (1933). Case II shows findings in conformity with previous reports. It is, however, included because in both these cases a striking tendency to symmetry of the lesions is observed. Although by no means constant, a number of illustrations of former cases confirm that this tendency is often seen, although it does not previously appear to have attracted comment. These cases also show the widespread nature of the disease, the long, the short and the flat bones having been affected. Both cases, also, show the appearance of the condition by the time of the end of treatment. In the first the patient was left with almost no radiological stigmata and in the second healing was most satisfactory. The condition can therefore probably be accepted as being relatively benign, and, particularly with modern therapy, it should be possible to give a reasonably confident prognosis of a satisfactory outcome.

## Summary

(1) Two cases of cystic tuberculosis are described.

(2) The main features of the disease are noted and stress is given to the simultaneous appearance of the lesions.

(3) The condition can, although rarely, affect adults. The present adult case exhibited a slighter reaction than that seen in children.

(4) Attention is drawn to the tendency of the lesions to be symmetrical in distribution and to be widespread, involving the long, the short and the flat bones.

(5) The prognosis is considered to be relatively benign.

I would like to acknowledge my gratitude to Dr. F. Campbell Golding for valuable advice in connexion with this subject, to Mr. G. K. McKee for providing details of the early history of Case II and to Mr. D. E. Macrae who treated Case I.

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# Neuropathic Lesions of the Feet in Diabetes Mellitus

By M. Mencer Martin, M.D., M.R.C.P.
*King's College Hospital*

Lesions of the feet in patients with diabetes mellitus occur with such frequency that the metabolic disorder is generally accepted as a predisposing factor. Occlusive peripheral vascular disease occurs at an earlier age in diabetics and is by many regarded as the major cause of foot lesions. Others have considered sepsis as mainly responsible. After investigating a large number of patients with various lesions of the feet it soon became obvious that insufficient attention had in the past been paid to diabetic neuropathy as an important factor.

Diabetic neuropathy is common in elderly diabetics because of the character of diabetes with onset in middle or later life. In the young the metabolic disorder starts acutely and treatment is soon required. In the elderly the disease is of insidious onset and slow progression, often remaining unrecognized for many years. There is time for complications to develop and elderly diabetics often seek medical advice not because of the classical symptoms of the disease but on account of complications of which neuropathy is a very common one (Martin, 1953*a*). This rather than vascular disease is believed to account for the high incidence of foot lesions in elderly diabetics.

Diabetic neuropathy affects mainly the nerves to the lower limbs at their periphery. Nonmyelinated nerve fibres appear to be involved early (Martin, 1953*b*) which predisposes to excessive trauma and lowers tissue resistance. Neuropathic lesions are thus most common about the toes and the bones and joints of the feet.

Cutaneous neuropathic changes commonly start as blisters and the deceptive lack of normal sensation leads the patient to ignore the lesion and delay treatment until secondary infection has resulted in extensive inflammation. Yet if the spread of infection can be prevented, healing occurs as the blood supply is often quite adequate (Figs. 1 and 2). In their more advanced form the neuropathic changes give rise to Charcot joints. In 1951 Parsons and Norton claimed that fewer than

Fig. 1.—The feet of a 58-year-old man with diabetic neuropathy, showing neuropathic soft-tissue lesions over the tips of both big toes. The lesions were painless and were noticed accidentally on removing the shoes.

Fig. 2.—The same lesions healed.

Fig. 3.—Right foot of a 60-year-old woman with shortened and thickened feet. There is tapering with marked atrophy of the distal parts of the metatarsals and changes in the metatarsophalangeal joints. The bones are well calcified and there is no evidence of ischæmia. The patient showed signs of peripheral nerve involvement and the appearances are in keeping with neuropathic arthropathy.

22 cases of diabetic arthropathy had been recorded in the world literature. Yet the incidence of such lesions in the diabetic population attending King's College Hospital was 0·22% which suggests that diabetic arthropathies must be more common that the paucity of reports would lead one to suspect.

Cases were reported of diabetic neuropathic arthropathies of the interphalangeal, metatarsophalangeal (Fig. 3) and midtarsal joints with disorganization of the joints and deformity of bones, but no evidence of bone resorption or infection and often with ossification of soft tissue surrounding the joint space. Generally neuropathic changes are of slow onset and gradual progression eventually resulting in a deformed foot. Arthropathy may, however, develop rapidly with sudden swelling as has been described in the classical arthropathy of Charcot (Martin, 1952).

The frequent association of cutaneous ulcers and neuropathic arthropathies has led a number of authors, notably Hodgson, Pugh and Young (1948) from the Mayo Clinic, to suggest that infection leading to osteomyelitis was the direct cause of the bone changes, independent of any associated nervous disorder. The denial of a nerve disturbance underlying the bone as well as the soft tissue lesion does not seem well founded, particularly as there is abundant evidence that damage to the nervous system does produce such lesions. Furthermore cases have been described with neuropathic arthropathies in the absence of skin lesions (Martin, 1952).

The recognition of diabetic neuropathy as a major factor in the causation of soft tissue as well as bone and joint changes in the feet of diabetics is of the greatest importance. There is good reason to believe that damage to autonomic and nonmyelinated pain fibres occurs much more frequently in diabetics than the incidence of clinically recognizable peripheral nerve involvement would suggest (Martin, 1953*a*). The presence of such nerve disease is believed to be basically responsible for a large proportion of the foot lesions in diabetics, and would explain the peculiar and chronic character of low-grade infection seen in the lower extremities of diabetic patients.

Purely neuropathic lesions are generally confined to joints and their prognosis as regards recovery is poor. However, most neuropathic arthropathies tend to become arrested and apart from the deformity cause little trouble. In progressive cases orthopædic appliances which prevent weight-bearing and further deformity may become necessary.

Where neuropathic changes are associated with occlusive vascular disease the treatment must be guided by the state of the peripheral circulation and is the same as for cases with peripheral ischæmia without neuropathy.

Recognition of diabetic neuropathy is most important where it has predisposed to sepsis in the presence of a good blood supply. The presence of nerve involvement modifies the character of the infection so that the changes found often appear most serious with extensive osteoporosis and apparent bone involvement. Yet as the blood supply is adequate, chemotherapy and local surgery, combined where indicated with peripheral vasodilator drugs, will often save a limb and leave a useful foot.

Perforating ulcers may present a problem, for although they tend to heal with rest, they frequently break down again when weight-bearing is resumed. This is due to faulty and often excessive weight-bearing by the ulcerated area and experience has shown that excellent and lasting results can be obtained by excision of the metatarsal head in the base of the ulcer.

The most important principle in surgery of the diabetic neuropathic foot in the presence of sepsis is never to close a wound but to leave the area wide open. Secondary suture is often possible a week or so later. Primary sutures frequently break down with spread of sepsis which necessitates longer hospitalization, often further surgery and may even endanger the limb.

With experience in the treatment of foot lesions in diabetics many more limbs can be saved which otherwise would come to grief.

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# Section of Neurology

President—MACDONALD CRITCHLEY, M.D., F.R.C.P.
(in the Chair)

[*September* 1, 1953]

JOINT MEETING WITH THE CANADIAN NEUROLOGICAL SOCIETY

MORNING SESSION

## The Pathogenesis of Cranial Nerve Palsies Associated with Intracranial Aneurysms

By H. H. HYLAND, M.D., F.R.C.P.(Lond.), F.R.C.P.(Can.) and
H. J. M. BARNETT, M.D., F.R.C.P.(Can.)[1]

CRANIAL nerve palsies accompanying intracranial aneurysms are common but there appear to have been few attempts to determine the pathological mechanisms leading to these palsies. For this reason we reviewed the cases with clinical evidence of cranial nerve involvement that had come to autopsy in recent years. Between 1940 and 1952, a total of 94 cases with aneurysms have been examined post mortem at the Toronto General Hospital and 39 had one or more cranial nerves involved clinically. Two groups were found: (1) those in which the aneurysm sac came in direct contact with the nerve and (2) those where the function of the nerve or its nucleus was disturbed by the secondary effects of hæmorrhage from aneurysm rupture.

TABLE I.—CRANIAL NERVE INVOLVEMENT

94 *Autopsy Cases of Intracranial Aneurysms*

| | No. of aneurysms | II nerve | III nerve | VI nerve |
|---|---|---|---|---|
| Direct involvement by aneurysms .. | 21 | 4 | 18 | 3 |
| Mechanisms secondary to hæmorrhage.. | 19 | 0 | 17 | 6 |

### DIRECT INVOLVEMENT BY ANEURYSMS

The first group consisted of 20 cases with 21 aneurysms directly involving 25 nerves, of which 18 were oculomotor, 4 optic and 3 abducens (Table I). While in this series it happened that only these 3 nerves showed clinical and pathological evidence of damage, it is possible, of course, for aneurysms to be so situated that they may directly involve any cranial nerve. Of these aneurysms, 17 arose from the anterior part of the circle of Willis, most commonly in relation to the internal carotid artery. There was definite evidence of extravasation of blood from all but 5 of the aneurysms.

Clinically and pathologically the evidence clearly indicates that impairment of the function of a nerve by a contiguous aneurysm occurs most frequently in conjunction with hæmorrhage. Thus in 16 of the 21 instances the onset or subsequent development of nerve palsy occurred in sudden episodes coincident with aneurysm bleeding. In histological studies of 15 of these nerves, 13 had fresh and 10 had old hæmorrhage in the substance of the nerve (Figs. 1 and 2).

[1]From the Departments of Medicine and Neuropathology, University of Toronto, and the Medical Service of the Toronto General Hospital.

Excepting those with terminal rupture and those with no rupture, the nerves were nearly always adherent to the aneurysm sacs. Fig. 3 shows the wall of a subclinoid aneurysm which is firmly attached to the degenerated III nerve. The patient had suffered his first attack of subarachnoid hæmorrhage six months before death. One month later he developed severe right-sided headaches which were accompanied by the abrupt onset of right III nerve paralysis, which persisted until his death from another cause.

In several instances the nerve was actually a part of the continuity of the aneurysm wall, as is shown in Fig. 4. In this case paralysis of the III nerve came on suddenly and completely with an attack of subarachnoid hæmorrhage ten weeks before death.

There was no evidence of bleeding from the 5 remaining aneurysms but with 2 exceptions the histories indicated that the nerve palsies had occurred in sudden episodes suggesting intraneural hæmorrhage. While there is no doubt that gradual compression through dilatation of a pulsatile aneurysm sac will damage nerve tissue, nerves so affected are evidently capable of surprising functional adjustment for a considerable time. However, an abrupt dilatation without rupture, such as evidently occurred in 2 of these aneurysms coincident with head trauma, could impair nerve function by mechanical stretching or it might lead to œdema or hæmorrhage in the involved nerve through venous obstruction, which would account for the sudden onset of the nerve palsies. Likewise in certain cases where rupture has occurred, the associated dilatation of the sac may be the major factor rather than the hæmorrhage. This was seen in a case of aneurysm at the bifurcation of the basilar, the aneurysm being deeply imbedded in the mid-brain (Fig. 5). In this case a partial left III nerve paralysis developed abruptly with the first attack of subarachnoid hæmorrhage two and a half months before death. Six days later, coincident with a second hæmorrhage, the III nerve paralysis became complete and a right hemiplegia appeared. The aneurysm evidently caused degeneration of the III nerve and cerebral peduncle by direct compression in 2 successive sudden episodes through dilatation of the sac which occurred with each of the 2 attacks of subarachnoid hæmorrhage. In contrast to those cases where nerves are involved after emergence from the brain-stem and may be capable of some adjustment, the nerve in this case was particularly vulnerable to compression because of the firm underlying mid-brain tissue.

There are clinical and pathological reasons for believing that when nerve palsies develop suddenly without being accompanied by frank signs of subarachnoid hæmorrhage, aneurysm leakage often occurs. This leakage of blood, or the accompanying acute dilatation of the sac, may provide the additional trauma necessary to cause loss of function in a nerve which has been able to function previously, although damaged by aneurysm pressure. Histological findings in the walls of aneurysms indicate 2 mechanisms by which dilatation, leakage and finally rupture may occur. It is common to find marked necrosis of the aneurysm wall in cases where bleeding has occurred and particularly where the sac is adherent to a nerve but in the wall of one unruptured aneurysm we found an area of bland necrosis (Fig. 6). Although necrosis such as this would be expected to lead to further dilatation and ultimately rupture, it may be caused initially by the nutritional impairment associated with stretching of the aneurysm sac. Another process which will cause dilatation, leakage and finally rupture is hæmorrhagic dissection of the sac. This was commonly seen in the intact portion of the walls of ruptured aneurysms and is probably the more important mechanism, although, of course, some degree of necrosis will precede dissection. Fig. 7 shows a section from an aneurysm which had previously leaked. This patient developed left-sided headaches and a III nerve palsy two months before death. Two weeks before death he became drowsy and developed a right hemiplegia following which his condition gradually deteriorated. Autopsy revealed a large, recently thrombosed aneurysm on the left posterior cerebral artery which was found to be severely compressing the mid-brain, left thalamus and left III nerve. There had been no gross rupture of the aneurysm but considerable blood had leaked into the adjacent tissues. There was a moderately severe internal hydrocephalus. The hæmorrhage, which can be seen dissecting the aneurysm wall, consisted of degenerated red and white blood cells and in the fibrous tissue between the thalamus and the aneurysm wall there was a large amount of phagocyted blood pigment. The leakage, which had occurred in the two months preceding death, was evidently determined by this dissecting process.

In all the nerves with hæmorrhage in their substance varying amounts of fibrous tissue proliferation were evident (Fig. 8). The fibroblastic proliferation, seen so consistently, is of interest in view of the clinical observation that no significant recovery of function of the affected oculomotor nerves had been noted in any of our cases, regardless of the duration of the nerve palsy. It would seem that the association of this fibrous tissue reaction with intraneural hæmorrhage prevents normal regeneration of the axis cylinders of the damaged nerves.

One of the most interesting findings was the lack of correlation between the duration of symptoms of nerve palsy and the amount of damage to the nerve found at autopsy. In some cases with short histories the nerves showed changes of a chronic type as well as the acute lesion. This evidence of pre-existing damage indicates the capacity of the nerves for functional adjustment to the effects of apposition to an aneurysm sac. However, such nerves will be vulnerable and the superadded acute

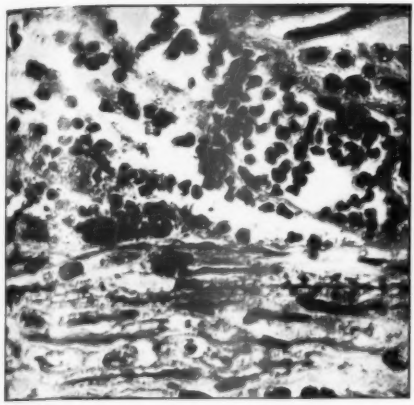


FIG. 1.—Oculomotor nerve showing old and recent intraneural hæmorrhage. The oculomotor paralysis had developed abruptly coincident with hæmorrhage from a carotid aneurysm five weeks before death. × 172.

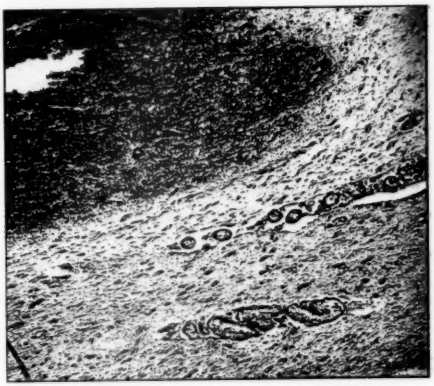


FIG. 2.—Anterior part of optic chiasma showing recent massive hæmorrhage and a diffuse proliferation of astrocytes. The patient had an aneurysm on the anterior communicating artery which had ruptured twelve days before death. × 26.

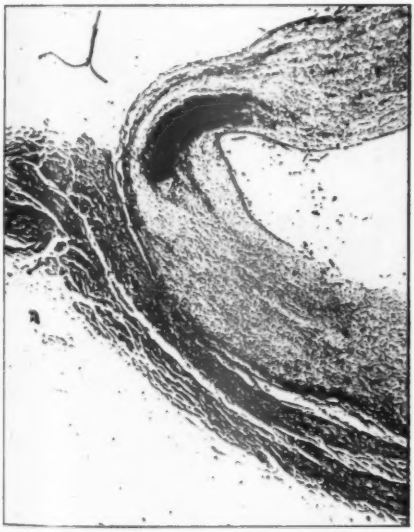


FIG. 3.—Wall of a carotid aneurysm and an adherent III nerve. The aneurysm wall is composed of thick fibrous tissue with hæmorrhage in the substance. The demyelinated nerve is firmly attached by fibrous tissue. × 14.

FIG. 4.—Wall of a ruptured carotid aneurysm containing ante-mortem thrombus. The degenerated III nerve is seen closely adherent to the sac on the right-hand side. The wall of the aneurysm terminates abruptly about the middle of the section and beyond this point the nerve alone forms the wall of the thrombus. × 30.

lesion determines the abrupt onset of clinical signs from which there may be no recovery. There were 6 patients, all of whom had symptoms of less than three weeks, with findings in the nerves indicating severe irreversible damage. The section seen in Fig. 8 is from a patient in this group. She developed her III nerve paralysis suddenly only nine days before death yet the severe, chronic nature of the lesion is evident. These findings explain why recovery after carotid ligation may be unsatisfactory in spite of a short history.

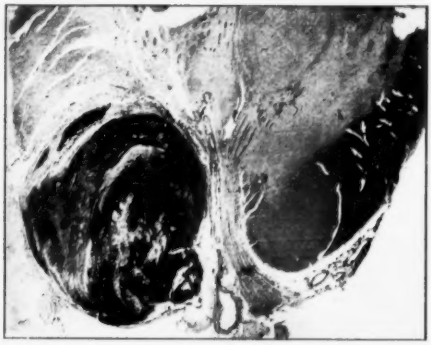


FIG. 5.—Transverse section of mid-brain to show destruction of III nerve and cerebral peduncle from compression by an aneurysm at the bifurcation of the basilar artery. A Weber's syndrome developed in 2 sudden episodes coincident respectively with the 2 attacks of subarachnoid hæmorrhage.

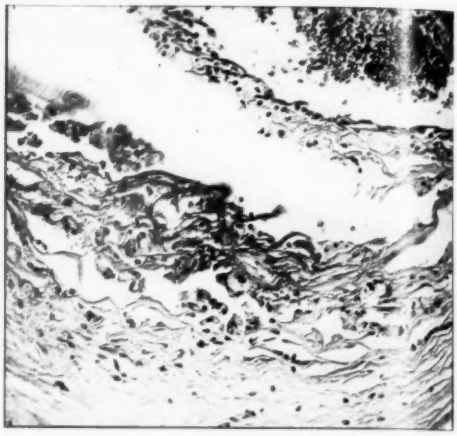


FIG. 6.—An area of bland necrosis in the fibrous tissue wall of an unruptured aneurysm. Numerous histiocytes are present but no inflammatory cells. × 117.

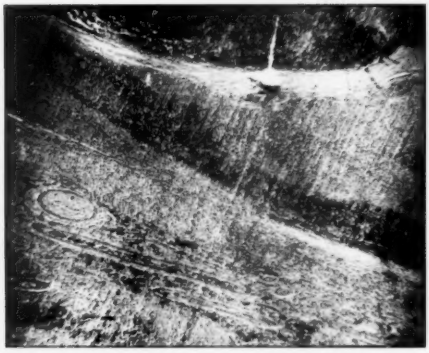


FIG. 7.—Vertical section through the wall of a thrombosed posterior cerebral aneurysm showing hæmorrhagic dissection of the wall. In the lower part of the section is a small, superficial portion of compressed, degenerate thalamus containing hæmorrhage. Between this and the aneurysm wall a thick layer of fibrous tissue, which contains phagocyted blood pigment, is obliterating the subarachnoid space. × 30.

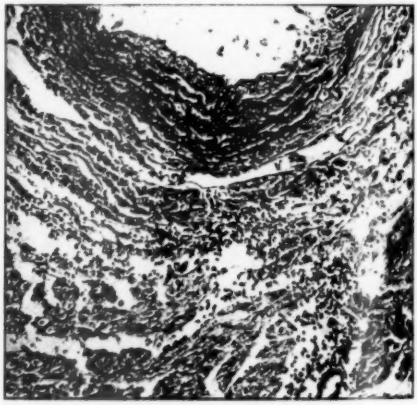


FIG. 8.—Section through the wall of a ruptured carotid aneurysm and the adherent III nerve. There is marked proliferation of fibroblasts in the nerve and between it and the aneurysm wall. Among the large fibroblasts are chronic and acute inflammatory cells, phagocyted blood pigment and red blood cells. The onset of symptoms had occurred nine days before death with rupture of the aneurysm. × 50.

## MECHANISMS SECONDARY TO HÆMORRHAGE

There were 19 cases of ruptured aneurysms in which secondary mechanisms had led to involvement of III and VI cranial nerves as indicated in Table I. Comparable to the former group of cases, 16 of these aneurysms also were situated on the anterior part of the circle of Willis. While these nerve palsies due to remote effects of hæmorrhage were almost as numerous, they contrasted with the former group by being often bilateral and usually terminal, developing at the earliest within the last two weeks of life. They were invariably found to be associated with severe aneurysm hæmorrhage and their development was therefore of serious prognostic significance.

Mid-line increased intracranial pressure hæmorrhages were found in the region of the oculomotor nuclei in the mid-brains in 5 instances to account for the oculomotor palsies. These patients all had ruptured aneurysms on the anterior part of the circle of Willis with intracerebral or subdural extension of the hæmorrhage. Fig. 9 is from a case of a ruptured anterior cerebral aneurysm with the main bleeding into the subdural space. The patient had partial bilateral III nerve palsies which were explained by the small mid-brain hæmorrhage. In addition to these 5 cases of anteriorly situated aneurysms, we have one case where hæmorrhage from a basilar aneurysm had caused secondary hæmorrhages in the mid-brain which were responsible for bilateral oculomotor palsies.

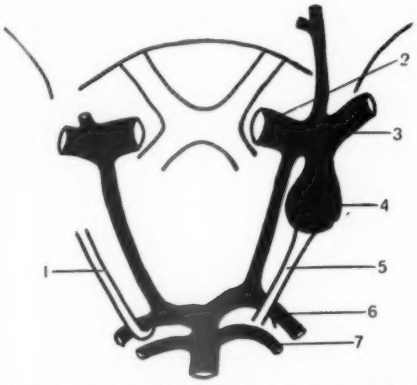
Another mechanism responsible for remote cranial nerve involvement was found in 2 cases with ruptured aneurysms situated on the internal carotid arteries. In each of these a contralateral III nerve

FIG. 9.—Sagittal section through the mid-brain showing a small mid-line hæmorrhage below the aqueduct, involving both oculomotor nuclei, in a case of ruptured anterior cerebral aneurysm.

palsy was found to be due to kinking and compression of the nerves by the posterior cerebral artery displaced when the brain-stem itself became displaced by the hæmorrhage (Fig. 10).

A third mechanism clearly responsible in 5 cases for ipsilateral III nerve palsies was pressure on the III nerve by a herniated hippocampal uncus. All 5 cases had intracerebral extension of the hæmorrhages.

There was a final group of 6 cases in which none of these more obvious mechanisms seemed to be in operation. However there was usually sufficient intracerebral hæmorrhage and associated œdema to account for considerable distortion of the brain-stem. This could lead to stretching of the




1. III cranial nerve.
2. Internal carotid artery.
3. Middle cerebral artery (pulled laterally).
4. Aneurysm.
5. III cranial nerve.
6. Posterior cerebral artery.
7. Superior cerebellar artery.

FIG. 10.—Diagram made from a case of ruptured carotid aneurysm with bilateral III nerve palsies. The aneurysm is seen directly involving the ipsilateral III nerve while the contralateral III nerve has been damaged through kinking and compression by the displaced posterior cerebral artery.

ipsilateral and contralateral III and VI nerves, to the point of functional impairment, as described recently in extradural hæmorrhage by Sunderland and Bradley (1953). In 2 of these cases the fourth ventricle and aqueduct were grossly distended with blood (Fig. 11). To account for the terminal bilateral oculomotor palsies in such cases one might speculate that in addition to the displacement of the brain-stem there was also an impairment of its function by sudden compression.


## Summary

In 94 autopsy cases of intracranial aneurysms there were 39 (40%) with clinical evidence of cranial nerve involvement. Pathological studies showed that the nerve palsies were caused directly by contiguous aneurysms in half the instances while the remainder resulted from secondary effects of the hæmorrhages.

In the first group the nerves come in contact with the aneurysms through dilatation of the sacs which may be accompanied by hæmorrhagic dissection or necrosis. The palsies result mainly from intraneural hæmorrhage consequent on aneurysm leakage or rupture. Fibrous tissue proliferation and adherence to the sac usually follow rapidly, leading to irreversible damage in the nerves. While nerves seem to be capable of considerable functional adjustment to the effects of compression by a gradually enlarging unruptured aneurysm, a sudden dilatation of the sac, with or without accompanying hæmorrhage, is likely to cause loss of nerve function. This may occur by mechanical stretching or by œdema or intraneural hæmorrhage from venous obstruction.

FIG. 11.—Hæmorrhage from a ruptured anterior communicating aneurysm with extension through the inferior surface of the frontal lobe, distending the ventricles with blood. The terminal bilateral oculomotor palsies may have been due to displacement and compression of the brain-stem.

Nerve palsies secondary to the effects of severe intracranial hæmorrhage from aneurysms were found to be caused by the following mechanisms: (1) mid-brain hæmorrhages resulting from increased intracranial pressure or from direct compression of the mid-brain by hæmorrhage from a posteriorly situated aneurysm, (2) kinking and compression of the contralateral oculomotor nerve through displacement of a posterior cerebral artery, (3) compression by herniation of a hippocampal uncus, (4) stretching or compression of the brain-stem due to sudden severe intracerebral and intraventricular hæmorrhage.

We wish to express our thanks to Professor E. A. Linell for allowing us full access to his autopsy material and records.

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# Post-traumatic Extenso-progressive Reflex Neurological Disturbances

By JEAN SAUCIER, F.R.C.P.(Can.)
*Professor of Neurology, University of Montreal*

A SYNDROMIC entity known as "post-traumatic extenso-progressive reflex neurological disturbances" has been reported by S. A. Barré in 1942 from cases that dated as far back as 1919.

This author then brought to the attention of neurologists histories of severe pain and important vasomotor changes occurring more or less rapidly after a trivial accident, together with gross sensorimotor impairment, more or less extensive in its distribution and out of proportion to the initial trauma. In the ensuing years, other cases, all occurring after a minimal traumatic insult, were reported in the French literature and elsewhere having the common features of reflex-like production, extension of the disorders to various degrees and lack of proportion between the external force and the catastrophic consequences that followed. Before 1942 many such cases were labelled as "undiagnosed" casualties.

Gradually, new cases that were apparently very dissimilar were added to the initial group because they behaved in the same reflex-like fashion, and because they extended rapidly and out of proportion to the initial trauma. The triple signature of the syndrome was then one of clinical, pathogenic and ætiological significance, and the nosographical entity was tentatively designated as "Post-traumatic extenso-progressive reflex neurological disturbances".

Reflex amyotrophies are classical acquaintances but they never serve as a pathognomonic warning; nor do the so-called reflex disturbances described by Babinski and Froment under the name of "Physiopathic troubles of reflex origin", although Barré includes them in the lighter types of his syndrome.

In 1905, Sicard described a syndrome "post-traumatic ascending neuritis" having certain features in common with Barré's cases. Sicard said the syndrome was the result of an infectious involvement of the corresponding spinal ganglia but he never mentioned any reflex activity. The histological picture was one of an interstitial reaction of the nervous trunks. In 1874, Weir-Mitchell had, perhaps, foreseen many of the clinical features of the syndrome but he failed to group them under a definite heading, and to outline the constant and characteristic elements of the clinical picture.

Clinical documentation of the past century is of little value because of its imperfect semiological technique and because many paralyses ascribed to reflex origin were actually caused by unrecognized foci of myelitis or to vitamin-deficiency polyneuritides.

Since 1919, descriptions of painful, amyotrophic and other clinical manifestations of extenso-progressive pattern have been published sporadically which support the reflex and irritative theory because no initial infection could be traced.

The syndrome often develops after a trivial wound, and, less frequently, after severe traumatic lesions of soft tissues, of bones, blood vessels and nerves, and finally, after certain *irritative lesions* of the nerves, especially of the sympathetic nervous fibres of a limb. Such traumatic alterations usually are localized peripherally, for instance, over the hand or foot, but they can also be observed at the proximal level; they can equally be localized on the sympathetic fibres of an intrathoracic or intra-abdominal organ, or over the free ending of a sensory cranial nerve or over the nerve itself. Signs and symptoms appear at once, or after a latent period, then they gradually extend involving, for instance, part of the limb, the whole limb, the ipsilateral other limb and even all four extremities. Such manifestations are, either in their intensity or in the speed of their spreading, out of all proportion with the initial cause. They frequently are excruciating pains which extend in the course of months or years to new areas; they are at other times clinically represented by hemiplegia, a limited torsion-spasm, tonic or tonico-clonic twitchings, Jacksonian epilepsy and even generalized epilepsy. Certain cases show syringomyelia-like syndromes or amyotrophic paralyses resembling lateral amyotrophic sclerosis. Other forms having the same chronological and circumstantial patterns and the same clinical progress have been described.

It is worth while to summarize at this juncture Barré's first observation:

His first case was that of a girl of 18 who came to him in May 1919 for pain in her left upper extremity. A few weeks after a mild trauma of the distal phalanx of her left middle finger she had felt transient but very intense pain over both sides of that finger which had slowly involved her wrist, forearm and arm while it spread to the whole hand and 5 fingers. Gradually the pain had become constant and had extended to the shoulder, to the left thorax, and, when the bouts were more severe, as far as the left hip. Such bouts were first infrequent but they soon occurred at shorter intervals; they could be brought on by certain movements or by a slight pressure over the left middle finger. The patient soon became somewhat of an invalid as she never used her left hand. She used to hold it in her right hand in a very careful fashion. She could hardly sleep. From the beginning, she had noticed that putting her left middle and ring finger in a glass of cold water had a soothing effect, and, like patients suffering from causalgia, she always kept a glass of cold water and sponges near-by. Her left hand appeared narrower than the right; the finger nails were longer and narrower, especially that of the middle finger; the skin was thinner and glossy; the thenar and hypothenar eminences were somewhat more flaccid than those of the right side and the forearm was a little thinner. However, during the periods of quiet, all movements were easy, and of normal amplitude; flexion and extension of the fingers were complete

and strong; adduction-abduction was good. Electrical reactions of nerves and muscles of the painful limb were normal. Tendon reflexes were normal and equal. Objective sensations were perfectly and equally identified but there was some hyperæsthesia to pin-prick over the whole left upper extremity. The left hand was warmer, more moist, more coloured and also more markedly pigmented; its veins were more apparent. One could also notice a left Horner sign which had been present a few weeks before admission but which was absent on photographs of the patient taken two or three years before.

The pilomotor reflex was essentially variable in its production and distribution. The oculo-cardiac reflex was paradoxically accelerated. The neurological examination was otherwise negative and a lumbar puncture did not reveal anything but normal findings. Blood pressure was 110/70 over both arms but oscillations were 2½ divisions less on the left side.

It was thought that those progressively ascending pains which were accompanied by vasomotor, temperature, secretory and oculo-pupillary dysfunction ought to be interpreted as the result of some sympathetic involvement closely related to excitatory impulses arising from the traumatized distal phalanx of the left middle finger.

Assuming that the irritating stimulus arising from the subungual region of the traumatized phalanx was carried along via the collateral nerves of the affected finger, a surgeon was requested to cut the collateral nerves of the finger and to sever the sympathetic plexuses of the collateral arteries. The operation, although incomplete, improved the patient considerably for a few weeks but gradually the former painful picture reappeared in its entirety. At the same time, the finger nail of the left middle finger was curving more and more sharply into the skin and it was examined for a cystic or neoplastic growth on April 26, 1920. The finger-nail was removed. The underlying pulp bulged very conspicuously; it was incised and an ovoid tumour was enucleated which measured 12 × 5 mm. It was this which gave the dome-like aspect to the finger-nail whilst at the same time it had depressed the bony phalanx, the periosteum of which had to be curetted in order to abolish all possible pressure over all nerve endings. After two or three days of excruciating pain the entire painful syndrome disappeared completely.

The patient remained one month at the clinic and during that time the Horner syndrome became less obvious while the temperature and circulatory asymmetry disappeared. The patient was seen ten years later with the same excellent results. The tumour was found to be a subungual neuro-myo-arterial glomus, as described by Professor Pierre Masson.

Since then many similar cases have been reported in the French literature. Apparently dissimilar cases have been added as they had the same ætiology and development, e.g. one of epilepsy due to peripheral irritation of traumatic origin which had been cured after the removal of neuromata from the right traumatized ring-finger; one of syringomyelia following a non-suppurative wound of the left wrist; one of amyotrophic lateral sclerosis after a slight laceration of the sole of the right foot by a rusty nail; one of ipsilateral hemiparesis and hemihypæsthesia after a superficial puncture of the dorsum of the left hand with a piece of barbed wire. Many other examples are now on record in the world literature.

Thus there is factual evidence of a vertical spread of neurological disorders, immediate or not, after a minimal peripheral wound of a lower or upper extremity. The two contralateral limbs may also present some abnormalities to a lesser degree.

## Conclusion

The mere perusal of those clinical documents logically invites one to group them together. It then becomes obvious that syndromes of various types may develop, either at once or later, after a minimal peripheral wound. Such syndromes extend to areas that widely overlap the initial lesion and may involve the two ipsilateral limbs, and even all four extremities. They are out of all proportion with their insignificant ætiology both in their intensity and spread and are frequently accompanied by violent pain and vasomotor disturbances. They may present themselves as hemiplegias, as torsion spasms, as Jacksonian and generalized epilepsy, as syringomyelias, amyotrophic lateral sclerosis, and as combinations of other manifestations. The original wound is usually trivial but it frequently involves the periosteum, a nerve or a blood vessel. The type of pain resembles what one observes in sympathetic involvement. Such wounds are usually localized over the distal extremity of a limb but they may also occur over the proximal extremity and even over the trunk. In most cases there was no suppuration and there was no reason to suspect a toxic origin. With these data in mind, a new syndrome has been described under the name of "Extenso-progressive neurological disturbances of traumatic origin due to peripheral irritation".

It is likely that this new nosographic chapter will develop into a more complete classification. It is also true that we shall not easily escape the necessity of changing our medico-legal thinking when we are confronted with post-traumatic pictures of this description. So far it is easily understood that the medico-legal expert has not yet paid much attention to certain serious neurological disturbances which followed minimal initial insults. He has been astonished and amazed, but, following the law of the lesser effort, he has discarded his embarrassment with a verdict of exaggeration or coincidence. In the future, however, the expert should wait and see; he should make a detailed inquiry into the initial phase of the disturbance, into the past of the victim and into the exact progressive pattern of the syndrome before he concludes for or against the claim.

Extenso-progressive manifestations may differ considerably in every way. Some have disappeared after surgery had removed the irritating cause. Others, deprived of the benefit of early surgery, developed syndromes resembling syringomyelia or amyotrophic lateral sclerosis. The following case of Lhermitte's was, fortunately, studied both clinically and histologically:

A man aged 66, showed marked deformities of the left hand with loss of the distal phalanges, loss of the little finger, scleroderma and an amyotrophy of the whole left upper limb including the shoulder. Motor, reflex and sensory disturbances were obvious, and, outlining the lateness of certain cases, all those signs had progressed slowly after repeated severe traumata of the left hand which had all been sustained in the course of one year, thirty years before. The patient having died of an intercurrent disease autopsy was performed and histological studies revealed a marked degeneration of the ulnar nerve at the wrist, which was less conspicuous at the elbow, and a decrease in the number of axons in the median nerve; these changes could be traced back in the posterior roots, in the lateral and posterior columns and in the posterior horns which were markedly atrophied. The extension of the lesions could also be found in the anterior horns, the cells of which had almost completely disappeared in the lower segments of the cervical cord; over segments C.7 and C.8 the volumetric reduction of the grey matter of the left half of the cord was striking. Finally, there were present many *myelinic neuromata* on the left roots from C.1 to T.1.

Whatever interpretation one wishes to give to these extensive changes which chiefly consist of a chronic irritation originating from the periphery and finally ending in degenerative changes, it does appear that such a case offers a striking demonstration of the low centripetal progression of peripheral lesions, and of the deeply seated terminal changes as well. Consequently, we can accept once for all that trauma can deeply modify the structures of the neuraxis as it seems also true that traumatic alterations are capable of an evolution that can be surprisingly lengthy, more especially the atrophic types.

The progression of lesions has not been so eloquently demonstrated for the traumatic types that resemble syringomyelia and amyotrophic lateral sclerosis and it is assumed that the histological changes that one will observe must differ from those in classical syringomyelia and amyotrophic lateral sclerosis of non-traumatic origin.

Neuropathologists should prepare for examinations and techniques of a new type whereby, at first, probably very minute changes will be demonstrated, particularly along the sympathetic pathways, but spreading by degrees to other pathways depending on the time the biopsy is made.

To explain their "physiopathic troubles of reflex origin", which, according to Barré, represent the minimal type of the extenso-progressive disturbances referred to in this paper, Babinski and Froment insisted on including the spinal cord in the reflex pathway. Whether the case was one of flaccid paralysis with amyotrophy or of contractures with hyperactive tendon-jerks, they concluded that there was a disturbance of the spinal centres. The short reflex, or axon-reflex can co-exist with a longer pathway reflex, the latter using sensory peripheral fibres, spinal ganglia and posterior roots, spinal centres, anterior roots and their efferent fibres. In a similar clinical syndrome it is highly possible that some elements may be produced by reflex interplays of different lengths. The fact of extensive reflex activity seems acceptable, if not certain. It is also usual to observe that the disturbances extend upwards until they reach the spinal centres. At that level the irritation bifurcates upwards and downwards, but chiefly upwards while it remains predominantly unilateral. It is as if the noxious irritation travelled centripetally, affecting the ipsilateral half of the spinal cord; it may then stop at that level, where the anatomical changes become organized, but in certain instances, as in Lhermitte's case, the lesions extend to the near-by segments, and more particularly to the upper levels; in such cases, the other half of the cord is frequently the seat of some damage. In other cases, the irritation reaches a much higher level, crosses the mid-line and creates histological modifications that may be reversible for a certain time. This would explain the reflex responses on the whole of one side of the body following an irritating stimulus arising from the distal extremity of one limb. It is not yet clear whether the irritation is conducted via the cerebrospinal nerves or via the autonomic fibres. Clinically both seem to be involved.

Although this *reflex* pathogenesis of extenso-progressive disturbances of traumatic origin is chiefly inferred clinically; although surgery, by removing the peripheral irritation, immediately stopped recent and relatively old troubles, as if through the extinction of the reflex activity; and although in Lhermitte's case histological lesions of the spinal cord could be seen, it does seem that complementary information is still necessary before the theory of reflex pathogenesis can be fully accepted. It is chiefly for this reason that I presented this paper.

The intense and prolonged response to a minimal peripheral irritation may be caused by the presence under the skin, near the periosteum, or in the wall of certain blood vessels of neurovascular corpuscles of the glomus type; it may be a momentary or constitutional state of the autonomic system with its conduction variability and pathological facilitation; it is certainly a problem of the unusual conduction of nerve impulse.

I have had the opportunity of studying a case which comes into the category of the widely extensive types:

R. L., aged 51, was admitted to the Hôtel-Dieu for more detailed observation from May 12 to June 13, 1953. I had followed him as a compensation casualty since May 1951. The accident occurred on February 2, 1951, when he cut his left hand over the thenar eminence with the cutting edge of a bricklayer's hammer. It was not a deep cut, hardly more than 5 mm. in depth and 2½ cm. in length. It was closed with 4 sutures and there was no infection. The closure was perfect seventy-two hours later, and even to-day one can hardly notice a fine white line over his left thenar eminence. The least pressure, however, over the scar is painful. The wound was considered so trivial that no hospitalization was thought necessary. Two days later, the patient felt some numbness, first at the site of the wound, then over the whole left hand and wrist; gradually, the numb feeling

was felt over the left forearm and elbow. Incidentally, he never returned to work. Three months later his left hand became weaker. His left lower limb never was numb but for the past three weeks (April 1953) the left calf has been the seat of unpleasant cramps. Six months after the accident the left upper limb, left side of the neck and face could not feel fine stimuli so sharply while the whole limb was weaker; later, it became numb in its entirety. Objective sensation remained normal over the left lower extremity. A few weeks after the accident there was some dysarthria, probably due to the left facial paresis. In the course of 1952 the left lower limb became slightly weaker. Taste and smell have been diminished since the second half of 1952.

As early as May 16, 1951, I had noticed that the scar was perfect in appearance but already a little painful; flexion and extension of the left hand were incomplete: the claimant could then hardly close his left hand and his handshake was very feeble; he could not adduct or abduct his left fingers; flexion and extension of the last three left fingers were fair but weak while flexion and extension of the left thumb and index could hardly be performed; abduction, adduction and opposition of the left thumb were decreased in a proportion of three-quarters. Sensation was fully preserved over the whole hand. Deep reflexes of the left upper limb were a little brisk but there was no Hoffmann sign. The neurological examination was otherwise negative. I was then very much perplexed and I ordered him to the rehabilitation clinic for physiotherapy with a strong feeling of a traumatic neurosis. Total temporary disability was maintained. Physiotherapy was found to be ineffective. Clinically, the picture was nearly the same except for a very definite and constant Hoffmann sign over the left thumb. Neurologically, there were no gross changes but a very slight hypæsthesia of the whole left upper limb. A partial permanent disability of one-third of his left arm was suggested.

On September 3, 1952, the patient told me that it had been impossible to find work because a good painter should be in full command of both hands, which, I realized, was true. Upon examination, the left hand was very much weaker and all movements were very awkward and feeble; deep reflexes were much more active over the left upper limb and the left Hoffmann persisted. There were no noticeable changes of the skin and the temperature and colour were that of the opposite limb. Objective sensation was grossly normal but the same slight hypæsthesia was still noticeable over the whole left upper extremity. I increased his P.P.D. to two-thirds of the functional value of his left upper extremity and I suggested the claim should be closed as I still remained prejudiced and thought there was a strong emotional component. I was certainly wrong because the patient came back to me at the Hospital Out-door Clinic and I had him admitted for further study three months ago.

My most recent examination is now summarized: when he walks he rapidly feels cramps over the left calf which last as long as he walks. His left lower limb is felt as heavier than the right. Motor power is decreased over all three segments of the left upper extremity, and more especially so over the left hand which has lost all practical working value. The same findings were elicited over the ipsilateral lower limb but to a lesser degree. Sensation, both superficial and deep, is decreased over the entire left side, including the face. Deep reflexes are definitely exaggerated on the left side but there is no ankle or knee clonus. Abdominals and cremasterics have almost disappeared on the left side. The Hoffmann sign persists and there is an equivocal left plantar extension. Vision is normal. There is partial anosmia and parosmia. Ocular convergence is incomplete, especially that of the left eye; the left corneal reflex is sluggish; the left face is hypæsthetic. Facial features are moderately deviated to the right while the forehead wrinkles equally well; the right eye closes more completely than the left. There is some slight dysarthria and some left hypoacusia but no nystagmus. The uvula deviates to the right and the soft palate is more flaccid on the left side. Head turning to the left is weaker. The tongue movements are slower and its tip deviates to the left. Cerebellum is unimpaired. A lumbar puncture gave normal readings. An EEG was negative. An EMG performed on muscles of the left upper extremity gave no evidence of a lower motor neurone involvement. The pneumo-encephalogram gave a picture of bilateral small foci of cortical atrophy.

To sum up, after a minimal cut of the left thenar eminence sustained thirty months ago, neurological disturbances started at once and extended progressively to the entire left side of the body under the aspect of both hemiparesis and hemihypæsthesia, as if the irritation had extended almost exclusively to the pyramidal and sensory tracts. The ætiological and chronological circumstances, the gradual extension and progression, the reflex-like march of events, all details point to the essentials of the syndrome described by Barré although this type does not correspond to the most commonly described picture.

I feel that I must revise my medico-legal opinion on this patient. Even if it seems too late to expect therapeutic success I should ask for a biopsy of his initial wound.

Of course, one should consider other ætiologies; on the other hand, one cannot escape noticing the striking sequence of events as one cannot deny the factor that has been a cause of constant irritation from the very beginning. I confess that I should have been less prejudiced and that, remembering irritative small wounds of the extremities I should have asked for an earlier biopsy during the weeks that followed the onset of this peculiar syndrome.

## Is Hepatolenticular Degeneration a Clinico-pathological Entity?

By J. G. Greenfield, M.D., F.R.C.P.

*From the Institute of Neurology, National Hospital, Queen Square, W.C.*1

Until 1948 the diagnosis of Wilson's disease rested on the characteristic motor symptomatology, associated with evidence, which was often slight during life, of cirrhosis of the liver. If familial incidence and a Kayser-Fleischer corneal ring were added the diagnosis was considered to be established. In 1948 new, biochemical signs were added to the picture of the disease; a peculiar amino-aciduria was found by Uzman and Denny-Brown and abnormal copper storage, which had been earlier noted by Haurowitz and Glazebrook, was confirmed by Cumings who suggested the use of BAL in treatment. This drug has since been used also in diagnostic tests.

Most cases of Wilson's disease which have been examined since this time have conformed to these biochemical criteria. This appears to be the case in all familial cases with a positive Kayser-Fleischer ring. So far, therefore, the old conception of Wilson's disease as a clinico-pathological entity has been confirmed. But there are also isolated, non-familial cases, resembling Wilson's disease in their motor and psychical symptoms and showing evidence of liver dysfunction, in which the typical biochemical changes are absent. Pathologically these cases resemble Wilson's disease in the type of tissue change in the nervous system but with quantitative differences. Such a case has recently been examined by Dr. Cumings and myself and forms the basis of this contribution.

The patient, Mrs. W. C., died at the age of 41 in St. Bernard's Hospital, Southall, and I am indebted to Dr. H. I. Coombs for the post-mortem material. Her history may be summarized as follows:

At the age of 5 she had an attack of jaundice. When aged 7 to 8 she had attacks of pain below the ribs on the left side with abdominal swelling and pyrexia, and the spleen was felt to be enlarged at the time. She was very ill for several months and until the age of 17 was never well enough to attend school regularly; the attacks of pain in the left subcostal region continued but became less severe. At the age of 21 she had appendicitis and peritonitis. She married at the age of 25. Her first pregnancy, about two years later, was accompanied by much œdema and resulted in a 10½ lb. stillborn baby. She had swelling of the legs during her second pregnancy when she was 28; this resulted in a 8½ lb. living child. After that she appears to have been fairly well until her third pregnancy, at the age of 34, during which she had again much general œdema, and which again resulted in a 10½ lb. stillborn baby.

At the age of 37 the severe stabbing pain below the left ribs returned and she went into Guy's hospital where the spleen was found to extend 4 fingerbreadths below the costal margin; it was hard and not tender. She was anæmic with 65% hæmoglobin. The hippuric acid test gave 49% of normal excretion; the thymol turbidity test was negative; serum bilirubin 1·25 mg.%; total serum protein 5·58%; globulin 2·9%; albumin 2·68%.

At the age of 38 she became psychotic with ideas of persecution and went into St. Bernard's Hospital for a week. At this time her speech was slow and deliberate, her gait unsteady and careful and there was intention tremor in both hands. A few months later she entered University College Hospital where examination showed absence of nystagmus and of any Kayser-Fleischer corneal ring. Tremor of the head and trunk on walking were now added to the clinical picture. Sir Francis Walshe found "the unusual combination of Parkinsonism and intention tremor sometimes seen in hepatolenticular degeneration but rare otherwise". The serum protein was then 6·6%; globulin 3·4%; albumin 3·2%. The urine was examined for abnormal amino acids by Dr. J. M. Walshe who found moderate excess of tyrosine, cystine and ethanolamine, as is not unusual in cases of severe hepatic cirrhosis. The heavy excretion of abnormal amino acids, usually seen in Wilson's disease, was not found.

At the age of 40 to 41 the movements of the neck and arms appeared to be more athetotic. The extensors of the right leg were paralysed with some wasting. There was variable patellar and ankle clonus with plantar responses of extensor type. She had several apoplectiform attacks with coma, lasting about two hours and considered to be attacks of hepatic coma. The blood pressure remained normal, 120/80. She died of bronchopneumonia at the age of 41.

At the post-mortem examination the liver was found to be much contracted, weighing 700 grammes; the surface consisted of raised lobules, each about 8 mm. in diameter, and similar lobulation was seen on the cut surface. The spleen was much enlarged, weighing 1,200 grammes. The brain weighed 1,238 grammes and showed considerable cortical atrophy in both frontal lobes. The left hemisphere and brain-stem were kept for histological examination. The right hemisphere was sent to Dr. J. N. Cumings for chemical examination. He found normal percentages of copper in all parts of the brain, as well as in the liver.

## Histological Examination

*Cortex.*—In the prefrontal cortex there is slight increase of neuroglial fibres in the subpial layer. In the deeper layers of the cortex many of the astrocytes have clear, oval nuclei with prominent nucleoli but no other chromatin except under the nuclear membrane. They measure up to 13 μ in the longer diameter. Some paired astrocyte nuclei are also seen. In one place where these large Alzheimer-like glial cells are specially numerous there is great loss of nerve cells, thickening of the capillary walls and increase in microglia. These areas look like small ischæmic lesions except for the condition of the astrocyte nuclei. There is no neuroglial fibrosis here. In other places, e.g. temporal cortex, there is a widened molecular layer containing many double and triple astrocytic nuclei, many being large and poor in chromatin. In the occipital cortex there is in places considerable nerve cell loss in the third, fifth and sixth layers where also there are many Alzheimer-like astrocyte nuclei, especially in the mesial cortex above the calcarine fissure. In the precentral cortex near the depths of the Rolandic sulcus there is a large oval finely granular mass, measuring 35 × 25 μ which may be a pyramidal cell of the 3rd layer distended with lipochrome granules. In its neighbourhood there is great shrinkage of the cortex so that all the layers of nerve cells are contracted together into a band which is thinner than the molecular layer.

*Basal ganglia.*—There is considerable shrinkage of the caudate and putamen, but no obvious loss of nerve cells or fibrous gliosis. Large astrocyte nuclei of Alzheimer type are more abundant here than in the cortex, and in some places there are as many of them as of nerve cells. In the inner section of the globus pallidus also there is an area where both nerve cells and myelin fibres are scanty

and large vesicular astrocytic nuclei are abundant. The nucleus caudatus is similar to the putamen but rather less affected. The largest Alzheimer nucleus seen in the putamen measured 15·5 × 10 μ. Very few of these large nuclei were surrounded by pigment granules. No neuroglial fibres staining with Mallory's hæmatoxylin were seen in the putamen, caudate or globus pallidus. No abnormality was found in the thalamus or nucleus subthalamicus (Luys). In the *substantia nigra* there is scattered melanin pigment, indicating some loss of nerve cells and many fairly large vesicular astrocytic nuclei are seen but here again there is no fibrous gliosis. No inclusion or neurofibrillary change was found here.

The *pons* and *medulla* show no abnormality.

The *cerebellum* shows no abnormality except astrocyte nuclei of Alzheimer type in the nucleus dentatus.

In this patient the history suggests that the liver was damaged at the age of 5 with resulting cirrhosis. From the age of 8 to 18 years there were recurrent attacks attributable to splenic enlargement. In the third and fourth decades other signs of liver damage became evident. Motor symptoms, an association of Parkinsonian rigidity with intention tremor, appeared at the age of 37 along with mild psychical symptoms. Attacks of hepatic coma came on at the age of 40 and the patient died at the age of 41. This history suggests that the cerebral damage was secondary to liver disease. Raymond Adams has shown that patients dying in hepatic coma, without previous nervous symptoms, have changes of Alzheimer type in the astrocyte nuclei of the basal ganglia and fronto-parietal cortex similar to those found in this case. It is difficult to believe that these glial changes may occur without any damage to the neighbouring neurons. Certainly in our case there was severe damage to the cortical nerve cells and also obvious damage to the substantia nigra. The neuronal changes in the basal ganglia were less evident, but in my experience they may not be very obvious even in typical cases of Wilson's disease.

Histologically, therefore, this case may be classed as hepatolenticular degeneration. although it was atypical in several respects, but chemically it was entirely different. There was none of the typical animo-aciduria, no abnormal copper storage and no Kayser-Fleischer ring. Cases like this are probably not very rare, but as the biochemical changes of Wilson's disease are recent discoveries they have not yet been reported. Their classification raises a difficult problem, since the biochemists exclude them from the category of Wilson's disease. The name *hepatolenticular degeneration* has never been entirely satisfactory since the cerebral changes in Wilson's disease are never limited to the lenticular nucleus, and a new classification and terminology seems to be needed. Meanwhile it is important that cases, such as this, which do not conform to the modern chemical criteria of Wilson's disease, should be fully recorded.

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## Copper Storage in Hepatolenticular Degeneration and Allied Diseases

By J. N. CUMINGS, M.D., F.R.C.P.

*From the Clinical Pathological Laboratory and the Department of Biochemical Research, Institute of Neurology, The National Hospital, Queen Square, London, W.C.*1

EXCESS copper has been found in the brains of patients suffering from hepatolenticular degeneration (Haurowitz, 1930; Lüthy, 1931; Glazebrook, 1945; Cumings, 1948; Spillane *et al.*, 1952). The urinary copper excretion has also been shown to be increased in this disease (Cumings, 1951; Denny-Brown and Porter, 1951; Spillane *et al.*, 1952; Matthews *et al.*, 1952).

Porter (1949) and Spillane *et al.* did not find any increased amino-acid excretion in the urine in a number of other nervous diseases such as Huntington's chorea, paralysis agitans, dystonia musculorum deformans and familial spastic paraplegia, but copper estimations in the urine in such conditions have not previously been recorded.

This paper gives the results found in the examination of 34 patients suffering from various disorders, including 3 new cases of hepatolenticular degeneration. The brains of 4 patients, one a case of hepatolenticular degeneration, have also been examined. In each of the 34 cases three twenty-four-hourly samples of urine were examined for copper by methods used previously, and for amino-acid nitrogen by the method of Albanese and Irby (1944).

Table I gives the diagnosis of 26 cases with the highest levels of copper and amino acid found. No chemical abnormality was found in any case.

TABLE I.—URINARY EXCRETION OF COPPER AND AMINO ACID IN SOME DISEASES OTHER THAN HEPATOLENTICULAR DEGENERATION

| Clinical diagnosis | No. of cases | Highest copper (μg./24 hrs.) | Highest amino acid (mg./24 hrs.) |
|---|---|---|---|
| Huntington's chorea | 3 | 120 | 280 |
| Cerebellar and extra-pyramidal | 2 | 92 | 250 |
| Kernicterus (late result) | 1 | 136 | 163 |
| Paralysis agitans | 1 | 80 | 319 |
| Disseminated sclerosis | 1 | 80 | 191 |
| Phenyl pyruvic acid oligophrenia | 2 | 140 | 212 |
| Tabes | 1 | 105 | 403 |
| Wernicke encephalopathy | 1 | 128 | 280 |
| Torsion spasm | 1 | 140 | 224 |
| Familial tremor | 1 | 74 | 414 |
| Chorea | 2 | 126 | 298 |
| Chorea athetosis | 2 | 90 | 310 |
| Basal ganglia spasm | 1 | 87 | 330 |
| Left hemisphere lesion | 1 | 85 | 176 |
| Gilles de la Tourette disease | 1 | 158 | 289 |
| Miscellaneous including dystonia musculorum deformans, hysteria, congenital chorea | 5 | 51 | 206 |

(All cases showed tremor.)

The results found in the 3 cases of hepatolenticular degeneration are shown in Table II. These cases had typical clinical signs and each showed a Kayser-Fleischer ring; all showed a very considerable excretion of both copper and amino acid in the urine far in excess of the normal. The first case gave a fourfold output of copper after BAL, but there was no alteration in the amino-acid excretion. Blood levels of copper in these cases were 115, 120 and 95 μg. per 100 ml. respectively,

TABLE II.—COPPER AND AMINO ACID URINARY EXCRETION IN HEPATOLENTICULAR DEGENERATION

| Case | Sex and age | Copper (μg./24 hrs.) | Amino acid (mg./24 hrs.) |
|---|---|---|---|
| F. K. | M. 25 | 330–500 | 851–1,070 |
| N. H. 43731 | M. 24 | 260–596 | 470–709 |
| C. L. | F. 15 | 560–690 | 500–900 |

(Examinations made for five to seven days on one or more occasions.)

while the second case showed 24 μg. per 100 ml. in the cerebrospinal fluid. The amounts of copper associated with the different globulins were estimated in one case by the method of Thompson and Watson (1949), and little difference from the normal was found.

Table III shows the results found in the remaining 5 cases. The first case, in addition to the cirrhosis of the liver proven at autopsy, had intermittent attacks of confusion and a tremor, but no Kayser-Fleischer ring was present. The second patient with cirrhosis, proved by biopsy, had no neurological

TABLE III.—COPPER AND AMINO-ACID URINARY EXCRETION IN 5 OTHER CASES

| Case | Sex and age | Clinical diagnosis | Copper (μg./24 hrs.) | Amino acid (mg./24 hrs.) |
|---|---|---|---|---|
| R. B. | M. 39 | Cirrhosis of liver | 80–162 | 190–240 |
| A. C. | F. 60 | Cirrhosis of liver | 100–156 | 224–243 |
| N. H. 39906 | M. 47 | Hepatitis. Motor neurone disease | 101–129 | 735–934 |
| N. H. 29441 | M. 31 | ? Jakob-Creuzfeld disease<br>? Westphal-Strümpell disease | 80–150 | 102–263 |
| N. H. 38397 | F. 25 | Diagnosis uncertain. ? Develop later into hepatolenticular degeneration | 84–104 | 145–250 |

signs. Neither of these cases showed any biochemical abnormality. The third patient had a tetraplegia with some dysarthria, but no Kayser-Fleischer ring. He had a chronic hepatitis following jaundice, but without a history of serum or blood transfusion. Although the copper excretion was normal, there was a well-marked amino aciduria, but without any specific amino acid predominating, as determined chromatographically. The fourth patient was one of a family of 6, 4 of whom had a similar clinical picture. Psychopathic traits, abnormal movements and dysarthria for some fifteen years, no Kayser-Fleischer ring and a normal liver on biopsy were the prominent features. Neither this patient—fully examined—nor the other 5 members of the family showed any biochemical abnormality. This would not appear to be a typical case of hepatolenticular degeneration, for one would have thought that with such a long history some biochemical abnormality in the urine would have been present. Case V had a history of an involuntary tremor of the left upper limb for fourteen months. No Kayser-Fleischer ring was found. Urine examinations were negative, but clinically it was thought that this case might develop into hepatolenticular degeneration at a later date.

The material examined after death came from 4 patients, and Table IV shows the results obtained. Only in the case of hepatolenticular degeneration was there any retention of copper in the tissues.

TABLE IV.—COPPER AND WATER CONTENT IN BRAIN AND LIVER

| Tissue | Parkinson M. 62 | | Cirrhosis liver M. 34 | | Cirrhosis, splenomegaly F. 41* | | Hepatolenticular degeneration M. 21 | |
|---|---|---|---|---|---|---|---|---|
| | Copper | Water | Copper | Water | Copper | Water | Copper | Water |
| Frontal cortex .. .. | 2·4 | 85% | 7·9 | 81% | 3·0 | 74% | 24·6 | 83% |
| Frontal white .. .. | 2·3 | 89% | 7·9 | 71% | 2·2 | 73% | 16·0 | 71% |
| Globus pallidus .. .. | 4·0 | 78% | — | — | 2·6 | 76% | 17·0 | 77% |
| Thalamus .. .. | 2·0 | 67% | 7·7 | 80% | 3·4 | 84% | 24·0 | 84% |
| Putamen .. .. .. | 2·8 | 80% | 8·0 | 78% | — | — | 20·0 | 84% |
| Caudate .. .. .. | — | — | — | — | 2·2 | 84% | 20·0 | 82% |
| Liver .. .. .. | — | — | 13·9 | 76% | 4·0 | 87% | — | — |

Copper in mg./100 grammes dry weight.

*This is the case described on p. 151 by Dr. J. G. Greenfield.

The tissues from 3 cases of multilobular cirrhosis of the liver have now been examined, and in none has there been an accumulation of copper in the tissues.

These results lead one to the view that, in a typical case of hepatolenticular degeneration with a Kayser-Fleischer ring, there is retention of copper in the brain and an increased urinary excretion of copper and of amino acids, and all 7 cases so far examined have shown this to be true. Other patients with a somewhat similar clinical picture, but without, in my experience, a Kayser-Fleischer ring, do not show any biochemical abnormality in the urine. These are not examples of an abnormal copper metabolism, and should accordingly be placed in a separate category. Considering the levels of blood copper in the 7 cases of hepatolenticular degeneration so far examined the lowest was 86 μg. per 100 ml. and the highest 150 μg. per 100 ml., with a mean figure of 116 μg. per 100 ml., while the figures for 21 of the other cases of both sexes recorded here ranged from 99 to 160 μg. per 100 ml., with a mean of 128 μg. per 100 ml.

No patient with any disease other than hepatolenticular degeneration has yet been seen having an increased urinary excretion of copper. This is true not only of neurological disorders, but also of 2 cases of proven multilobular cirrhosis of the liver and 1 of chronic hepatitis with jaundice.

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# Intractable Pain

By FRANK TURNBULL, B.A., M.D.[1]

## INTRODUCTION

HEREIN I propose to develop three propositions about Intractable Pain. They are points of view that have arisen from experience rather than experiment.

Explanation of the adjective "intractable" is necessary as a start. The word suggests a continuing state that is difficult to manage, or clearly unmanageable. Its application should be limited to painful conditions that accompany incurable disease. A useful arbitrary definition is: "continuing pain associated with incurable disease that requires for alleviation at least one daily dose of narcotic drug." Patients are included within this category when their continuing pain is severe, and is not relieved by non-narcotic drugs. An obvious criticism of this limited operational definition is that it does not take into account the differences of individual reaction to pain.

## BACKGROUND

The most frequent occurrence of intractable pain in association with organic disease is the combination of pain and advanced cancer. My observations apply to this relationship. I will refer to the British Columbia Cancer Institute which is across the street from the Vancouver General Hospital. Since this Institute opened in 1939 the responsibilities and the scope of the neurosurgical consultant have never been defined, a happy circumstance that is largely responsible for the development of these ideas.

Early experience with the treatment of intractable pain associated with cancer indicated that the details of specialized technique, though important, did not present the major problem. A greater need was the ability to recognize when the pains of cancer had become a permanent state, or better still, which cases of cancer were going to develop intractable pain. This consideration led one to the more basic problem—"why do they develop".

A Pain Clinic was initiated at the B.C. Cancer Institute. Patients with certain types of cancer were examined periodically provided that they first applied for treatment of cancer without any complaint of pain. An attempt was made to assess the circumstances of the individuals who eventually developed intractable pain, in contrast to the status of those more fortunate individuals whose disease, if incurable, terminated with only a brief state of cachexia. That early programme languished during the war, but served as a pilot plan. Our present major study concerns the development of pain associated with cancer of the cervix.

(That is the background story. Now, the three principal arguments.)

## THE ARGUMENTS

(1) When intractable pain develops after all definitive treatment for the primary disease has terminated, it is in the best interest of the patient to regard pain as a disease in itself.

(2) Treatment of this disease—i.e. intractable pain—in a large cancer centre, should be under the direction of a neurologist, either surgical or medical, who should have wide responsibility.

(3) The criterion of success for any specific form of treatment or for any plan of general management, in a given case, is the percentage of the total terminal pain period that is relieved.

## INTRACTABLE PAIN AS A DISEASE

In spite of the universal interest in cancer research, there is still a surprising lack of factual data about the relative frequency and the average duration of intractable pain. A round-robin enquiry was made some years ago to my gynæcological colleagues in British Columbia, concerning the frequency of intractable pain in the end stages of cancer of the cervix. It was recognized that the gynæcologist's responsibility for the disease lay chiefly in the realm of diagnosis, and that the end stage is usually treated by a general practitioner. But no group could be expected to have a wider acquaintance with the literature. Their replies about the frequency of intractable pain varied from "negligible" to "100%".

The records of 100 fatal cases of cancer of the cervix were studied for data about pain. They had received treatment for their cancer consecutively between 1939 and 1942. A number of this group had been examined at our initial Pain Clinic. The time coincided with my early questionnaire to the gynæcologists. The survey indicated with certainty that 38% suffered intractable pain. An additional 14% were listed as probable cases. The average duration of intractable pain among the certain cases was seven months.

[1]Associate Clinical Professor of Surgery (Neurosurgery), University of British Columbia Medical School, Vancouver, B.C., Canada.

When one reconstructs, from the records, the chain of events that ensues after intractable pain becomes established, the most common-to-all and striking feature is the lack of a planned course of treatment—psychological, sociological, and medical. Fruitless search for secondary cancer continues even after conclusive evidence of incurable recurrence is established. There is a well-organized therapy for the cancer itself, but when hope of cure has vanished the plan peters out. It is during this stage that intractable pain is most frequently initiated. The patient is passing out of the care of the surgical specialist or radiotherapist and back into the hands of the general practitioner. The doctor in general practice is usually well able to handle the problem of terminal cachexia, or a brief bout of intolerable pain that can be managed by purposeful narcotic addiction. But a prolonged period of intractable pain is apt to become a sordid story.

The stage is set when deep, boring, agonizing pains, which do not respond to simple sedation, and which prevent sleep, become established in a patient who has completed the definitive treatment for cancer. It is time for an orderly review. A search is indicated for complications such as radiation necrosis, fistula, intestinal or ureteral obstruction. Treatment of these complications naturally follows if there is reasonable hope of thereby relieving the pain. If pain persists, and evidence of recurrent cancer is clear, then no spontaneous relief is in sight. It is time for a new Plan. It is now in the best interest of the patient to regard the pain as a disease in itself.

## The Control of Intractable Pain

What arguments may be advanced to justify the placing of this disease under the direction of a neurologist? Chiefly because no other specialty is as fully trained to view the disease (intractable pain) in its entirety. Secondarily, because the neurologist has almost no place in the active treatment of those forms of cancer that may be complicated by intractable pain, and therefore enters into the care of each of these patients with a fresh viewpoint. Under his guidance there should be in every large Cancer Institute a Special Treatment Clinic.

The first responsibility of the Special Treatment Clinic is to search out and keep under active review all the cases of intractable pain. In the review of 100 fatal cases that I have mentioned, it was surprising to learn that one's ability to utilize some form of effective treatment for intractable pain had only been tested in one-third of the cases who actually suffered intractable pain. "Out of sight, out of mind" was the usual position for the consultant on the problems of pain.

The next responsibility of the Clinic is the co-ordination of specialist with general practitioner services and of hospital with home. At all stages in the patient's course there should be provision for access back to the Special Treatment Clinic if original plans or treatment cease to result in effective control of the pain.

The director-neurologist needs to be familiar with the relative merit of every form of symptomatic treatment for pain. A review of his efforts with any one form alone will always provide him with a lesson in humility.

## Criterion of Success

When one recalls the clinical story of a patient who has received gratifying relief from intractable pain by special treatment, it is seldom without regret that definitive treatment to arrest the pain was not undertaken earlier. A consideration of the total pain period will provide one with the true perspective. The report of one month, or six months, of terminal relief, by this or that therapy, is a record of technical success—but may only represent a short appendix to a long story of clinical failure.

The phrase "terminal pain period" is an important qualification on any claims about the success of treatment. Relief that stops short of the end, even by a few weeks, will satisfy no one but an enthusiastic recorder. The patient, his relatives and the general practitioner will quickly forget a pleasant interlude if pains recur. Memories for pain are etched deeper than those for pleasure.

## Summary

This has been a very sketchy attempt to present some arguments about intractable pain. It is a specific form of derangement with characteristic symptoms. A special organization is necessary for adequate detection and control. The best criterion of success is the patient's viewpoint.

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Dr. Denis Williams' paper on **Stupor Caused by Brain-stem Lesions** will be published in *Brain*.